SECTION VI

MATERIAL IMPAIRMENT: CARDIOVASCULAR DISEASE

CARDIOVASCULAR DISEASE

Introduction

This submission is set forth in two parts. Part I provides a critical evaluation of the claims and literature cited by OSHA in its Proposed Rule on the issue of ETS exposure and cardiovascular effects. Part I concludes that OSHA has not provided an adequate scientific foundation for its position that ETS exposure in the workplace increases the risk of adverse cardiovascular effects. Of particular importance is that OSHA has not based its position on the best available evidence, namely those epidemiological studies that actually attempted to estimate workplace ETS exposure in relation to heart disease risk. The best available evidence does not support a claim that workplace ETS exposure is associated with an increase in heart disease risk.

Part II provides a compilation of literature which raises questions about whether ETS exposure is associated with adverse cardiovascular effects. Most of this literature, despite its importance and relevance, was not even cited by OSHA. The literature in Part II includes conclusions from several major reviews. It also includes reports on several specific areas discussed incompletely or inadequately in OSHA's comments on cardiovascular disease. These areas include discussions of the extremely low levels of ETS or of ETS constituents to which

nonsmokers might be exposed, as well as reports discussing research suggesting that any measurable cardiovascular responses to ETS are minor.

Part I: Response to Specific OSHA Claims

OSHA HAS NOT PROVIDED AN ADEQUATE SCIENTIFIC FOUNDATION FOR ITS POSITION THAT ETS EXPOSURE IN THE WORKPLACE INCREASES THE RISK OF ADVERSE CARDIOVASCULAR EFFECTS

The major discussion of cardiovascular effects in OSHA's Proposed Rule is provided at Section II.C.4. (59 FR 15977) The following discussion relates primarily to that section, although other portions of the notice are addressed as well, when warranted by their relevance to cardiovascular disease claims.

OSHA argues that research indicates that ETS exposure has a variety of adverse cardiovascular effects, including both acute effects, relating especially to oxygen supply and demand, and chronic effects, such as atherosclerosis and increased risk for the development of and death from coronary heart disease.

OSHA does not provide adequate support for its claim that ETS in the workplace should be regulated because of an association between ETS exposure and adverse cardiovascular effects. Much of the supporting literature cited by OSHA deals with active smoking, not ETS. Other studies, even though they may deal with ETS, are so flawed and limited in scope that they do not provide a sound basis for cardiovascular disease claims. Perhaps most importantly,

actual workplace data on ETS and heart disease are scant. Such data as exist do not support an association between workplace ETS exposure and cardiovascular disease.

OSHA DOES NOT BASE ITS CONCLUSIONS CONCERNING WORKPLACE ETS EXPOSURE AND HEART DISEASE RISK ON THE BEST AVAILABLE EVIDENCE. BASED ON THE BEST AVAILABLE EVIDENCE, WORKPLACE ETS EXPOSURE HAS NOT BEEN ASSOCIATED WITH A STATISTICALLY SIGNIFICANT INCREASED RISK OF HEART DISEASE.

Since OSHA's proposed rulemaking relates to the workplace, the best available evidence it should consider on the issue of heart disease risk and ETS exposure is that based on the workplace, not on residential exposure or spousal smoking. Of the epidemiological studies cited by OSHA relating to ETS and heart disease, three studies provided data on workplace exposure. These are: Dobson, et al. (Ex. 8-85); Lee, et al. (Ex. 8-191); and Svendsen, et al. (Ex. 8-295). Each of those reports provided estimates of the relative risk for heart disease mortality associated with workplace ETS exposure. The studies were consistent in not reporting a relationship of workplace ETS exposure with heart disease. Therefore, based on the best available evidence, the literature does not support OSHA's claim that workplace ETS exposure is related to heart disease in nonsmokers.

The three workplace studies are discussed more fully below.

Dobson, et al. (1991)

Dobson, et al., was a case-control study of myocardial infarction and heart disease mortality, which included questionnaire data relating to coworker smoking as an estimate of workplace ETS exposure. Odds ratios, with 95% confidence intervals, for workplace ETS exposure were reported as follows: 0.95 (CI: 0.51-1.78) for men and 0.66 (CI: 0.17-2.62) for women. Based on these data, Dobson, et al. concluded that the "odds ratios for passive smoking at work did not suggest increased risk."

Lee, et al. (1986)

Lee, et al., reported a hospital-based case-control study in which, in addition to information on spousal smoking, ETS exposure was estimated by asking the subjects about the extent to which they were exposed to ETS in four situations: at home, at work, during daily travel and during leisure time. Using a numerical index which combined questionnaire responses on ETS exposure in each of these situations, Lee, et al., reported relative risks of 0.52 (for lower combined exposure) on 0.61 (for higher combined exposure). Lee, et al, did not provide confidence

intervals, but stated that none of these risks ratios were statistically significant.

Svendsen, et al. (1987)

This study, although it primarily used spousal smoking as the estimate of ETS exposure, also included a small amount of information regarding workplace ETS exposure, as estimated from questionnaire data relating to smoking by coworkers. Comparing nonsmokers whose coworkers smoked to nonsmokers whose coworkers did not smoke, the following relative risks, with 95% confidence intervals, were reported for heart disease. For coronary heart disease mortality, the relative risk reported was 2.6 (CI: 0.5-12.7) and for fatal or nonfatal coronary heart disease combined, the relative risk reported was 1.4 (CI: 0.8-2.5). The wide confidence intervals include 1.0 and are, therefore, not statistically significant.

In sum, the best available evidence does not support the claim that workplace ETS exposure is associated with an increased heart disease risk. None of the three epidemiological studies cited by OSHA that include workplace data on ETS exposure and heart disease report a statistically significant association. Moreover, the relative risks in two of these studies are less than 1.0 (relatively fewer deaths in the ETS exposed workers).

OSHA provides inadequate support for its claims about ETS exposure and thrombus formation

OSHA addresses the issue of thrombus formation in the Proposed Rule at Section II.C.4.(a). (59 FR 15977)

OSHA argues that ETS exposure is involved in the formation of blood clots. OSHA cites only two laboratory studies to support this claim. Both of these studies focused on platelet activity. In one of these, Burghuber, et al. (1986) (Ex. 8-40), examined platelet function in a group of only nine nonsmokers, following a single exposure to high levels of ETS. The relevance of this artificial, short-term laboratory procedure to actual workplace conditions is highly speculative. Furthermore, these authors acknowledged that their test for platelet function in the laboratory may have no relevance to how platelets act in real life. They stated: "However, as with other platelet function tests, we do not know if this **in vitro** procedure accurately reflects platelet function **in vivo**." (p. 37) The authors further acknowledged that it was not known whether their research had implications for cardiovascular function in ETS-exposed nonsmokers. They stated: "Further investigation is needed to elucidate whether this finding is important with respect to a possible increased incidence of thromboembolic disease among non-smokers passively exposed to cigarette smoke." (p. 37)

In another laboratory study cited by OSHA on ETS exposure and platelet function, Davis, et al. (1989) (Ex. 8-80), reported that 20 minutes of exposure to ETS increased platelet aggregation and also increased the number of endothelial cell carcasses in the blood. However, this was a highly limited study of only 10 male subjects, for which there was no true control condition. More specifically, in their exposure condition, the nonsmokers sat for 20 minutes in a hospital corridor where patients typically smoked. Not only does this constitute an imprecise ETS exposure, but it is not comparable to the control nonexposure condition. In the nonexposure condition, the nonsmokers sat in a laboratory where smoking was not allowed. A hospital corridor and a hospital laboratory are entirely different environments, involving potential confounding factors such as social conditions, noise factors, ventilation factors and a variety of other differences.

Other than the two laboratory studies, the only other citation with ETS data cited by OSHA was a 1991 report by Dobson, et al. (Ex. 8-85) This epidemiological study, in addition to reporting odds ratios for ETS exposure and heart disease, also provided data on fibrinogen concentrations. However, Dobson, et al. repeatedly noted that there was no statistically significant association of fibrinogen concentration with ETS exposure. Moreover, limitations of this study were explicitly acknowledged by the authors, thus making this paper unreliable as a basis for

OSHA's claims. For example, Dobson, et al. noted that there were "[d]ifferences in the methods of data collection and truthfulness in reporting smoking habits" between their exposed and nonexposed groups and that this might "have lead to bias." (p. 796) The potential effects of confounding factors, especially socioeconomic status, were noted, as well as the lack of statistical power in their study. In general, with regard to their epidemiological procedure, which was the basis for both the odds ratio and fibrinogen data, Dobson, et al. stated: "On balance, the effects of bias and confounding could have lead to overestimation of risks due to passive and active smoking." (p. 796)

Other citations listed in OSHA's review of the thrombus formation issue are not relevant to ETS. Some merely provide background or theoretical information concerning cardiovascular disease processes. (e.g., Exs. 8-111, 8-272) Others are studies of active smoking, not ETS. (Exs. 8-157, 8-224)

OSHA fails to adequately support its claim that ETS exposure is associated with vascular wall injury

OSHA addresses the issue of vascular wall injury in the Proposed Rule at Section II.C.4.(b). (59 FR 15977)

OSHA argues that ETS exposure may harm the endothelial lining of the arterial wall, but provides almost no support for this claim. In connection with this claim, OSHA refers to only one citation -- namely, the Davis, et al. (1989) report (Ex. 8-80), which, as noted in the previous section regarding thrombus formation, is a highly limited and flawed study.

OSHA's discussion of possible mechanisms of effect is not adequately supported; some of the cited references are irrelevant to this issue

OSHA addresses the issue of possible mechanisms of effect primarily in the Proposed Rule at Section II.C.4.(c). (59 FR 15977) Part of OSHA's discussion of risk assessment in Section IV.F.2, which addresses cardiovascular effects in relation to pharmacokinetic modeling, is also germane.

In Section II.C.4.(c), OSHA argues that there are three mechanisms by which ETS exposure "may place stress on the heart." The first mechanism is by decreasing myocardial oxygen supply. The primary manner in which ETS exposure theoretically might have this effect, as discussed by OSHA, is via formation of carboxyhemoglobin. OSHA cites only one study on this issue which actually involved ETS. This was a 1978 report by Aronow. (Ex. 8-13) The Aronow study is widely regarded in the scientific literature as being methodologically weak and unsubstantiated.

Furthermore, it is important to note that Aronow has been criticized severely for unethical and dishonest scientific practices, to the extent that the government no longer relies on his data. (Shephard, R., The Risks of Passive Smoking, London, Croom Helm Ltd., 73, 1982.) (Mintz, M., "FDA, Citing Phony Evidence, Bars Drug Tests by Researcher," The Washington Post, March 23, 1983.) (Peterson, C., "EPA Probe Criticizes a Study Used in Air-Quality Standard," The Washington Post, June 7, 1983.)

Although OSHA cites several additional reports in the context of discussing oxygen supply and demand (Exs. 8-242, 8-323, 8-324), these are reports on cigarette smokers, not of nonsmokers exposed to ETS.

The second mechanism for placing "stress on the heart" mentioned by OSHA is that oxygen demand may be increased via nicotine. However, OSHA does not provide any citations demonstrating that there is an association of ETS exposure with myocardial oxygen demand, much less an association with an increased demand specifically as a result of nicotine in ETS. Perhaps there is a theoretical argument, based on claims that nicotine is a pharmacological stimulant, for speculating that ETS may be associated with increased oxygen demand. Such an argument, however, does not recognize that the amounts of nicotine in ETS are extremely small and of doubtful physiological or cardiovascular

relevance. [See Part II.B. of this submission for examples of literature, ignored or not adequately addressed by OSHA, which relates to the minute levels of ETS, and of ETS constituents, to which nonsmokers might be exposed, and the doubtful cardiovascular significance of such exposure levels.]

The third mechanism discussed by OSHA is that ETS exposure may influence the cellular ability of the heart to utilize oxygen for energy production. The only citation on this point provided by OSHA is Ex. 8-123, which OSHA describes as a study demonstrating that healthy subjects became fatigued quicker when exercising in the presence of ETS. However, OSHA's description of Ex. 8-123 is incorrect. Ex. 8-123 is not a study of exercise performance and ETS. It is not even a research report with original data. It is merely a draft of a review paper by Stanton Glantz and William Parmley. In one section of their draft manuscript, Glantz and Parmley discuss an exercise study involving healthy subjects and ETS. This 1985 study by McMurray, et al. is elsewhere referenced by OSHA as Ex. 8-217. However, the McMurray, et al. report does not provide direct measurements of cellular oxygen utilization. Thus, it does not bear importantly on the issue for which OSHA cited it.

An additional heart disease mechanism proposed to be related to ETS is suggested by OSHA in Section IV.F.2., where

cardiovascular physiology is discussed in the context of pharmacokinetic modeling of ETS exposure. In Section IV.F.2., in addition to carbon monoxide and nicotine, OSHA proposes that polycyclic aromatic hydrocarbons (PAHs) have been associated with cardiovascular effects. To support this claim, OSHA cites the draft manuscript by Glantz and Parmley (Ex. 8-123), which presents no original data. It references several reports primarily dealing with injections of massive amounts of PAHs into chickens and pigeons. Given the doses and manner of administration, it is highly questionable whether this type of study has implications for any sort of inhalation exposure related to tobacco smoke, whether active smoking or ETS exposure.

OSHA's discussion of acute heart effects relies heavily on studies of questionable validity and fails to accurately represent the conclusions of some reports

OSHA addresses the issue of acute heart effects in the Proposed Rule at Section II.C.4.(d). (59 FR 15977-8)

In this section, OSHA argues that ETS exposure has certain acute effects, such as raising CO levels in the blood, increasing heart rate and blood pressure and affecting blood components that may be involved in atherosclerosis. Much of this section duplicates the claims in OSHA's immediately preceding

section on "Possible Mechanisms of Effect." OSHA again relies strongly on highly flawed studies, in particular, the 1978 Aronow study (Ex. 8-16, which is the same as Ex. 8-13) and the studies on platelets by Burghuber, et al. (Ex. 8-40) and Davis, et al. (Ex. 8-80).

One of OSHA's central points in this section is that exposure to ETS results in a significant increase in carboxyhemoglobin. It is odd that, in introducing this topic, OSHA cites the review and conclusions of the National Research Council (1986). In fact, the NRC report concluded that if background air has little or no carbon monoxide, then even upper estimates of what might be produced from ETS would "have a negligible effect on carboxyhemoglobin levels." (p. 128) Furthermore, the 1986 Surgeon General's Report, in addressing this same issue, concluded as follows: "Thus, small increments of carbon monoxide due to environmental tobacco smoke may be indistinguishable from that due to endogenous and non-tobacco-related sources." (p. 202)

OSHA also incorrectly describes that data in Guerin, et al. (Ex. 8-129) as indicating that it is common for workplace ETS exposure to be associated with significant increases in COHb levels. In point of fact, Ex. 8-129 concludes the opposite, noting that "studies which quantified the percentage COHb in nonsmokers show very little difference in nonsmokers who were or were not

exposed to ETS." (p. 160) Elsewhere in Ex. 8-129, a similar conclusion is reached, noting that nearly all CO in indoor environments arises from sources other than ETS.

> CO has been measured repeatedly in rooms where there is adequate ventilation, with and without cigarette smoking. In many cases, the difference in values is small, and is easily masked by either normal variation in the data or the precision of the analytical measurement. Studies which measure the concentration of COHb in both ETS-exposed and non-exposed subjects is consistent with environmental CO measurements, and have demonstrated no consistent significant differences in most indoor environments. The chief difficulty is interferences from other sources of CO, particularly cooking, heating, and vehicle exhaust. One author (Eatough, 1988) states that about 90% of all CO arises from sources other than ETS. (p. 177) (Ex. 8-129)

Other literature cited by OSHA in this section also does not provide substantial support for, and sometimes is, at best, remotely relevant to OSHA's claims of acute cardiovascular responses to ETS. For example, OSHA cites Ex. 3-38 to support its claim that ETS has acute effects in angina patients. However, Ex. 3-38 consists of materials from the state of Washington, Department of Labor and Industries, relating to a proposed indoor air regulation. It has no apparent relevance to the context in which OSHA cited it. On the same point, OSHA cites Milhorn (1989). (Ex. 8-222) But Milhorn (1989) is not a study of ETS. It is

primarily a review of behavioral issues related to nicotine, as they might be relevant to physicians' advice to their patients about smoking.

On the issue of potential cardiovascular responses in healthy people, OSHA cites Asano, et al. (1985) and McMurray, et al. (1985). (Exs. 8-18 and 8-17) Although these articles report minor changes in certain cardiovascular variables, such as heart rate, it is doubtful whether these have any physiological significance, even assuming that such responses were actually direct responses to ETS, rather than reflective of a psychological reaction to ETS exposure.

In supporting its claim that ETS exposure has acute effects on blood components, OSHA again cites Burghuber, et al. (Ex. 8-40) and Davis, et al. (Ex. 8-80), which as noted repeatedly above are very weak, especially relative to the scientific weight OSHA is urging them to carry.

OSHA claims that effects of ETS exposure "may be additionally aggravated by simultaneous exposure to other compounds." In support, OSHA cites Ex. 3-446, which consists of comments from a government employee's labor union, and appears to provide no substantive information on this issue. On this same point, OSHA cites a 1988 review by Eriksen, et al. (Ex. 8-99) This

is perplexing, since the conclusions in Ex. 8-99 generally track those in the 1986 National Research Council and Surgeon General's Reports, namely, that data on the issue of ETS exposure and cardiovascular effects are methodologically weak and unconvincing.

There are several reports and reviews, not considered or not adequately taken into account by OSHA, which have addressed the issue of potential cardiovascular responses to ETS. Selections from this literature are set forth in Part II.C. of this submission, indicating a sizeable body of scientific data and opinion questioning a role of ETS or of ETS constituents in acute cardiovascular effects.

OSHA's discussion of epidemiologic and experimental data does not adequately support claims of an increased risk of chronic heart effects associated with ETS exposure in the workplace; OSHA fails to critically review cited studies; OSHA misrepresents the nature of available data

OSHA addresses the issue of chronic heart effects in the Proposed Rule at Section II.C.4.(e). (59 FR 15978-9) Epidemiologic literature on this issue is also reviewed in the context of its risk assessment, at Section IV.B. (59 FR 15992)

In Section II.C.4.(e), OSHA provides a single paragraph discussion of the epidemiologic studies relating to ETS and heart

disease, coming to the conclusion that these studies indicate a "modest impact" of ETS exposure on heart disease, with relative risks in the range of 1.3 to 2.7.

OSHA cites the following epidemiological reports.

Ex. 8-85, Dobson, et al. (1991)

Ex. 8-120, Garland, et al. (1985)

Ex. 8-138, He, et al. (1989)

Ex. 8-139, Helsing, et al. (1988)

Ex. 8-142, Hirayama (1984)

Ex. 8-148, Hole, et al. (1989)

Ex. 8-154, Humble, et al. (1990)

Ex. 8-191, Lee, et al. (1986)

Ex. 8-277, Sandler, et al. (1989)

Ex. 8-295, Svendsen, et al. (1987)

Contrary to OSHA's claim, the 11 citations given by OSHA in support of its conclusion do not report a consistent association of ETS exposure, usually inferred from spousal smoking, and heart disease risk. In studies where questionnaire estimates were obtained concerning workplace exposure, the data are especially weak on the issue of a possible association of ETS exposure and heart disease risk.

OSHA's misleading use of the 11 epidemiologic reports it cites on ETS and heart disease is evident in the manner in which these reports are grouped in Table IV-2. (59 FR 15993) In two instances, once in the "Positive" column and once in the "Equivocal positive trend" column, OSHA cites the same study twice. In the "Positive" column, both Helsing, et al. (Ex. 8-139) and Sandler, et al. (Ex. 8-277) provide essentially the same data on ETS and heart disease. In the "Equivocal positive trend" column, Gillis, et al. (Ex. 8-122) report preliminary data later reported by Hole, et al. (Ex. 8-148) Listing all four reports, when only two studies are represented, gives the impression that more "positive" data are available than in fact might be the case.

It is of special interest that two of the studies on ETS and heart disease cited by OSHA as "positive" or with an "equivocal positive trend" reported data using questionnaire estimates of workplace exposure. However, neither of these studies provides data suggesting an association of workplace ETS exposure and increased heart disease risk.

One of the studies with workplace data, Dobson, et al. (Ex. 8-85), is categorized by OSHA in Table IV-2 (59 FR 15993) as "positive." However, in this study, for ETS exposure at work, the odds ratios and 95% confidence intervals were 0.95 (0.51-1.78) for men and 0.66 (0.17-2.62) for women. Dobson, et al. concluded:

"The odds ratios for passive smoking at work did not suggest increased risk." (p. 793)

In another report, categorized by OSHA as having an "equivocal positive trend," Svendsen, et al. (Ex. 8-295) collected a "limited amount" of data on workplace ETS exposure. Study participants were asked about the smoking habits of their coworkers. Comparing nonsmokers whose coworkers smoked to nonsmokers whose coworkers did not smoke, the following relative risks (with 95% confidence intervals) were reported for heart disease.

-- Coronary heart disease death - RR = 2.6 (CI 0.5-12.7)

-- Fatal or nonfatal coronary heart disease - RR = 1.4 (CI 0.8-2.5)

Svendsen, et al. also reported data on a potential joint effect of coworker smoking plus spousal smoking, for the endpoint fatal or nonfatal coronary heart disease. Relative to nonsmoking men, neither whose wives nor coworkers smoked, the following risks were reported.

-- Both wife and coworkers smoked - RR = 1.7 (CI 0.8-3.6)

-- Wife smoked, but coworkers did not - RR = 1.2 (CI 0.4-3.7)

-- Wife did not smoke, but coworkers did - RR = 1.0 (CI 0.5-1.9)

In sum, all relative risks pertaining to workplace ETS exposure (either alone or in combination with spousal smoking) were not statistically significant.

OSHA incorrectly lists Hirayama (Ex. 8-142) as a "positive" study in Table IV-2. (59 FR 15993) While one of Hirayama's tables (Table 5, p. 183 of Ex. 8-142) appears to contain a statistically significant risk ratio for one subgroup of nonsmoking women married to smokers, Hirayama did not report an overall relative risk. Using Hirayama's data, however, Lee (Lee, P.N., Environmental Tobacco Smoke and Mortality. Karger, New York, 1992) recently calculated this ratio to be a nonstatistically significant 1.15 (95% C.I.: 0.94-1.42). (Lee, 1992, p. 187)

Very little weight can be given to the He, et al. study (Ex. 8-138), since it is a minor Chinese-language report based on

only 34 heart disease cases. As noted previously, the Sandler, et al. (Ex. 8-277) report is not relevant since it repeats the data in Helsing, et al. (Ex. 8-139) Also, as noted, the Dobson, et al. report (Ex. 8-85), actually reported nonstatistically significant relative risks less than 1.0 insofar as workplace data are concerned. This leaves OSHA's conclusions on increased heart disease risk based on a single "positive" epidemiological study, Helsing, et al. (Ex. 8-139)

As is typical of ETS epidemiological studies, Helsing, et al. suffers from weaknesses, such as unreliable ETS exposure estimates, and failure to attempt to control for confounding factors. The issue of unreliable exposure estimates is a particular problem for Helsing, et al., because the smoking status data were collected in 1963 and then used to classify subjects during the 12 years following. Many changes probably occurred in smoking behavior during the subsequent 12-year follow-up. This concern was noted by the authors.

> All smoking data were obtained in the 1963 census, so no provision can be made for changes in smoking habits which we know took place as a result of publicity about health effects of smoking. (p. 921)

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Other changes in the compositions of the households may have occurred during the follow-up period. Although the authors

assume that any changes might influence the ETS comparison groups randomly, this is mere speculation.

> We also have no data on changes in the household composition which may have occurred prior to or after 1963. Thus, we implicitly assume that any such changes occurred randomly in the population. (p. 921)

Although an attempt was made to adjust statistically for some potential heart disease risk factors (age, sex, etc.), no data were available on many potentially important risk factors for heart disease, such as diet, exercise, blood pressure and cholesterol.

> We have very little data on other risk factors for arteriosclerotic heart disease in the study population. . . . other factors such as diet and exercise might differ in families with and without smokers; we cannot ignore the possibility that such differences could influence our findings. (p. 921)

In sum, the epidemiological literature cited by OSHA as providing "positive" evidence of an ETS and heart disease association provides an extremely weak scientific basis for such a claim. After excluding incorrectly cited literature (Sandler, et al.; Hirayama), a small-scale foreign report of uncertain reliability (He, et al.) and research which, in fact, challenges a workplace ETS exposure/heart disease claim (Dobson, et al.), OSHA

is left with a single supporting citation (Helsing, et al.), which itself is highly flawed.

The problems with Helsing, et al. are particularly troublesome for OSHA's case, because OSHA's risk estimate for heart disease deaths associated with ETS (Section IV.D., 59 FR 15995-6), depends entirely on the Helsing, et al. data for its relative risks. OSHA ignores or glosses over the study's weaknesses relating to ETS exposure, classification of smoking status and confounding factors. Furthermore, without adequate foundation, OSHA states matter-of-factly that the Helsing, et al. study "can be generalized to the general public," conveniently failing to acknowledge that the Helsing, et al. study was performed in a single county in a single state in the U.S.

In addition to epidemiologic reports, OSHA also uncritically cites a number of laboratory and clinical reports or reviews, many of which were designed to examine active smoking and do not even relate to ETS. Other studies which purport to relate to ETS are cited by OSHA as fact without any serious attempt to evaluate their scientific validity.

For example, OSHA provides a substantial amount of detail concerning a recent study said to show that ETS exposure increases myocardial infarct size in rats and increases atherosclerosis in

rabbits. In this context, OSHA incorrectly describes a 1993 report by Zhu, et al. (Ex. 8-330) as relating to infarct size in rats, when, in fact, Ex. 8-330 is a rabbit study of atherosclerosis. The rat infarct study described by OSHA appears to be a 1994 report by Zhu, et al. (Zhu, B., Sun, Y., Sievers, R.E., Glantz, S.A., Parmley, W.W. and Wolfe, C.L., "Exposure to Environmental Tobacco Smoke Increases Myocardial Infarct Size in Rats," Circulation 89(3): 1282-1289, 1994.) Neither the 1994 Zhu, et al. report on rat infarcts, nor the report on atherosclerosis in rabbits cited by OSHA (Ex. 8-330) meet basic standards of scientific control. Both involve excessively high levels of smoke exposure, which was sidestream smoke, not ETS. The conditions of exposure also left a stress factor uncontrolled, which is particularly important in heart disease research.

To examine the 1994, Zhu, et al. report in more detail, it is clear that it is not even relevant to ETS. It apparently involved simultaneous exposure of groups of rats, up to 24 at a time, to extremely high levels of sidestream smoke, not ETS, in an unventilated exposure chamber. The average air levels of nicotine (1103 $\mu g/m^3$) and carbon monoxide (92 ppm) are several orders of magnitude higher than would be observed in even the most extreme human smoking situation. Moreover, a group of confined rats together in a chamber pumped full of smoke to the point where breathing was almost impossible is going to experience stress in

direct proportion to the extent of exposure. Any test for myocardial infarction is going to be influenced by such a stress factor. In short, the Zhu, et al. study is probably more of a study of stress than a study of ETS.

In an effort to support OSHA's claim that ETS adversely affects "blood components," OSHA denotes nearly half a column to a 1985 report by Olson. (Ex. 8-245) Olson reports that excessive exposure to intense levels of only weakly diluted sidestream smoke in rats can substantially elevate COHb levels. However, the Olson report did not even pertain to heart disease; it was a study of lung enzymes. It involved high concentrations of sidestream smoke, not ETS, which is a highly dilute mixture. Furthermore, it is clear that the exposure conditions were not relevant to COHb levels associated with ETS, when even literature cited by OSHA indicates that COHb levels in ETS-exposed nonsmokers are essentially indistinguishable from nonexposed nonsmokers. (Guerin, et al., Ex. 8-129, discussed under "Acute Effects.")

The Davis, et al. report (Ex. 8-80) on platelets and endothelial cells is again cited, despite its lack of an adequate control condition.

OSHA cites two Czechoslovakian reports to support a claim that ETS exposure affects cardiac cellular metabolism.

(Gvozdjakova, et al., 1984, Ex. 8-130; Gvozdjakova, et al., 1985, Ex. 8-131) Both of these studies are from the same laboratory and involve an experimental model in which rabbits were apparently exposed to mainstream cigarette smoke for periods of up to eight weeks. The authors claim that this smoke exposure adversely effected myocardial mitochonchial respiration. This is suggested as a mechanism underlying cardiomyopathy in smokers. Although the model involved "passive" inhalation of smoke by the rabbits, it is clear from the levels and nature of smoke delivery, and from the authors' explicit comments, that this research was intended to apply directly to heart disease in smokers, not to ETS.

Benowitz (1991) (Ex. 8-25) is cited several times to support claims about nicotine and carbon monoxide. This citation, however, does not deal with ETS. It is a review of nicotine in the context of smoking and delivery of nicotine via nicotine gum or via transdermal patches. Likewise, the Muscat, et al. (1991) report (Ex. 8-234) on lipid profiles deals with smokers, not ETS.

Leone, et al. (1991) (Ex. 4-196) is cited as support for a claim that CO decreases ventricular fibrillation threshold. The Leone, et al. report did not provide data on ventricular fibrillation, much less any data about CO and ventricular fibrillation in particular.

Conclusion

In conclusion, OSHA's discussion of cardiovascular effects is replete with incorrectly cited literature, misinterpreted or uncritically-examined studies and blatant errors as to the relevance of OSHA's citations to the claims advanced. Thus, OSHA has failed to make its case that ETS exposure in the workplace is associated with heart disease risk. The best available evidence is data on workplace ETS exposure and heart disease risk. To the extent that workplace ETS exposure data are available, an association with heart disease risk is not supported.

Part II: Additional Literature Ignored or Not Considered Adequately by OSHA

OSHA OMITS A NUMBER OF RELEVANT REVIEWS AND STUDIES FROM THE PROPOSED RULE; THESE REFERENCES FURTHER UNDERMINE CLAIMS THAT ETS EXPOSURE IN THE WORKPLACE IS ASSOCIATED WITH A SIGNIFICANT RISK OF HEART DISEASE

A. Literature reviews challenging claims of ETS-associated risk

The literature contains several literature reviews which conclude that a potential relationship of ETS exposure and heart disease has not been established. In view of the highly limited data on workplace ETS exposure, it is not surprising that none of these reviews provide conclusions specifically focusing on the workplace. However, these reviews do address broad problems with the ETS/heart disease data. If such data are generally inconclusive, then they are reasonably viewed as also specifically inconclusive in regard to the workplace. OSHA failed to recognize the conclusions of these reviews.

U.S. Department of Health and Human Services (1986)[1]

This review examined the available data and judged that "no firm conclusion" (p. 10) could be made regarding a possible relationship between ETS and heart disease.

Committee on Passive Smoking, Board on Environmental Studies and Toxicology (1986)[2]

This committee report stated that any potential heart disease risk related to ETS would be "difficult to detect or estimate reliably" from epidemiological studies, and would be "the same order of magnitude as what might arise from expected residual confounding due to unmeasured covariates." (p. 263)

Wexler, L.M. (1990)[3]

At a ETS conference held at McGill University in 1989, Lawrence Wexler, of the New York Medical College, concluded that recent data did not provide a basis for altering the earlier conclusions by the Surgeon General and National Research Council concerning ETS and cardiovascular disease.

> Based on the available evidence, it is this author's opinion that it has not been demonstrated that exposure to ETS increases the risk of cardiovascular disease. (p. 139)

Weetman, D.F. and Munby, J. (1990)[4]

Two scientists from the University of Sunderland, United Kingdom, reviewed the literature on ETS and heart disease and presented their conclusions at an international conference on indoor air quality held in Lisbon, Portugal in April 1990.

> It is concluded that no increased risk of cardiovascular disease can be associated unequivocally with exposure to ETS, and it seems probable that this will continue to be the case until specifically designed trials are instigated, and some objective measure of degree of exposure can be devised. (p. 215)

Weetman, D.F. (1993)[5]

In a subsequent conference, which addressed a variety of reported risk factors for heart disease in nonsmokers, Professor Weetman again reviewed the ETS and heart disease issue. His review focused on the epidemiological literature, and emphasized that major flaws in the available studies made it impossible to draw conclusions as to any possible association of ETS exposure and heart disease.

> It is not possible to conclude that a risk to cardiovascular health has been established from the epidemiological studies considered in this paper. Each of the studies is flawed in at least one major way. If there are to be more studies, and the importance of cardiovascular diseases suggests there should be, one can only hope that they will be conducted in a careful and objective way. (pp. 134-135)

Thiery, J. and Cremer, P. (1990)[6]

Two physicians from the University of Munich, Germany, presented their conclusions at an international conference in Hungary in June 1990.

> Taking into account the small increase in coronary risk in passive smokers as compared to non-exposed subjects and also the low validity and small number of epidemiological studies available and the fact that their results are at least inconsistent, a relationship between passive smoking and cardiovascular diseases cannot be established on these data. (p. 6)

Armitage, A.K. (1991)[7]

In a 1991 book discussing a wide range of issues involving ETS, the literature on heart disease was reviewed by Alan Armitage, former director of toxicology of a major European research laboratory and head of pharmacology at the Tobacco Research Council Laboratories in the United Kingdom. He judged that the scientific data have not established an increased heart disease risk in nonsmokers exposed to ETS.

> It is clear that the evidence for a harmful effect of ETS in enhancing CHD [coronary heart disease] risk in non-smokers is not very convincing. . . . (p. 114)

Armitage, A.K. (1993)[8]

In a subsequent review in 1993, Armitage, writing as a consultant pharmacologist and toxicologist, expressed a similar evaluation of the ETS/heart disease literature.

> On the current evidence a causal relationship between exposure to ETS and the development of CHD has not been proved. (p. 27)

Caldwell, A.D.S. (1993)[9]

Armitage's 1993 review appeared in the Journal of Smoking-Related Diseases. In an editorial in the same journal issue, A.D.S. Caldwell, the journal's managing editor, emphasized that the issue of confounding variables was of particular importance in the case of heart disease. This is because of the hundreds of factors reportedly associated with the disease. Caldwell observed that the numerous heart disease risk factors make it extremely difficult to make confident statements about a potential role of ETS.

> But assessing the impact of ETS is an exercise made hazardous by confounding variables lurking around every statistical corner. In the case of CHD, for example, some 300 risk factors have at some time or other been identified -- by what means is it possible to unravel these data and point the finger with any degree of confidence at ETS per se as a major causative element?

Lee, P.N. (1991)[10]

In 1991, Peter Lee, an independent British statistical consultant, published a critical analysis of the epidemiological literature relating to ETS exposure, cancer and heart disease. In the area of heart disease, he was particularly critical of the risk

assessments by Wells (1988) and Kawachi, et al. (1989). Both of these risk assessments concluded that ETS is associated with a large number of heart disease deaths annually. Lee challenged this conclusion, and agreed with the 1986 National Academy of Sciences and Surgeon General's reports, in that both considered the ETS/heart disease data inadequate.

> In the risk assessment by Wells, heart disease deaths formed 70% of the total. In that by Kawachi et al, they formed 89%. As noted above, in 1986 none of the major authorities considered that ETS had been shown to cause heart disease. Evidently Wells and Kawachi, in assuming that ETS causes heart disease, are jumping to a conclusion that a number of panels of distinguished scientists have not reached. While there are more data now than in 1986, it remains abundantly clear that the evidence still does not support this conclusion. (p. 199)

> Although it has been demonstrated above that the risk assessment for heart disease essentially rests on the results from two studies, both of which seem unreliable, a number of other general points can be made. First, there are a very large number of risk factors for heart disease. It is evident that adjustment for these factors in the studies has always been incomplete, and often seriously incomplete. Second, the extent of the association seen in some of these studies, which in some cases is close to that reported in relation to active smoking, is implausibly high when viewed against the extent of the association seen in relation to active smoking. Third, there is a major danger of publication bias. It is notable that the literature is still relatively sparse despite the numerous ongoing studies of heart disease and the fact that heart disease in a non-

> smoker is probably 50 times or so more common than lung cancer in a non-smoker. (p. 200)

Lee, P.N. (1992)[11]

In 1992, Peter Lee published a more detailed, book-length review of the epidemiological literature on ETS exposure in relation to mortality and several diseases. In his view, various weaknesses and biases in the data precluded the ability to draw any conclusion as to the potential association of ETS exposure and heart disease.

> Mainly because of the problems caused by the strong likelihood of severe publication bias, it cannot be concluded from the existing evidence that ETS is associated with heart disease. The present author understands that the American Cancer Society intends to publish within the next year or so findings related to ETS based on its second large prospective study. It is hoped that results from its first prospective study will also be released. Until there is such evidence, and hopefully also evidence from other studies involving substantial numbers of deaths from heart disease with good control of confounding and with evidence on ETS exposure from sources other than the spouse or in the home, it is certainly premature to come to any conclusions. (pp. 195-196)

Huber, G.L. Brockie, R.E. and Mahajan, V.K. (1992)[12]

Gary Huber, M.D., of the University of Texas Health Center, in collaboration with two other physicians, recently reviewed the literature relating to claims that ETS is associated

with increased heart disease risk. These authors described the epidemiological studies as "inconsistent" and considered the magnitude of the risks reported in these studies to be "within the range of 'background noise.'" Huber, et al. also emphasized the point that potential confounding variables have not been adequately controlled in studies of ETS exposure and heart disease.

> The studies should be viewed with healthy scientific skepticism because they have not been controlled adequately for numerous confounding factors potentially important to the development of these diseases. (p. 32)

Aviado, D.M. (1992)[13]

In 1992, Domingo Aviado, M.D., a consultant with Atmospheric Health Sciences in Short Hills, N.J., published an extensive review of environmental tobacco smoke in the context of heart disease in the workplace. He did not consider the data supportive of an association of workplace ETS exposure with heart disease, and emphasized the low levels of ETS constituents to which workers might be exposed.

> It is the opinion of this author that the available studies do not support a judgment that ETS exposure is associated with any form of occupation-related heart disease. Although ETS reportedly contains constituents that have been associated with occupational heart disease, the concentrations are so low that it is unlikely for any substance to attain the

corresponding TLV (threshold limit value) in a work environment. (pp. 475-476)

Aviado, D.M. (1993)[14]

In 1993, Dr. Aviado again addressed this issue, concluding that "the available studies do not support a judgment that ETS exposure is associated with any form of occupation-related heart disease." (p. 130)

Crépat, G. (1992)[15]

G. Crépat, a scientist at the University of Dijon, France, reviewed the literature relating to ETS exposure and heart disease, in a presentation at an international indoor air quality meeting in Athens, in April 1992. He concluded that the relative risks for ETS and heart disease reported in epidemiologic studies have probably been overestimated and are not explained by the available "physiobiochemical" data.

> This suggests that mean RR [relative risk] of CHD due to ETS exposure calculated from available epidemiologic studies, has probably been overestimated as at the moment it cannot be explained by physiobiochemical changes caused by ETS in the body. (p. 440)

B. Literature emphasizing low levels of ETS constituents

One way to approach the question of ETS and heart disease is to examine the levels of ETS to which nonsmokers might be exposed. Reported levels of exposure to carbon monoxide may be particularly of interest in view of the potential role some authors have speculated it to have in heart disease. The literature provides many examples of reviews concluding that potential nonsmoker ETS or CO exposure levels are extremely low and not likely to be of physiological significance. The conclusions of several notable examinations of this issue are extracted below.

Adlkofer, F.X., Scherer, G., Von Meyerinck, L., Von Maltzan, Ch. and Jarczyk, L. (1989)[16]

> COHb in passive smokers rises only slightly above the normal physiological level so that it is difficult to differentiate from COHb-values measured in non-exposed non-smokers. (p. 185)

Cole, P. (1981)[17]

> Another source of CO is the inhalation of exhaled tobacco smoke and sidestream smoke from other smokers, called 'passive smoking'. In a City office adjacent to Barts, where smoking was allowed, we measured the COHb levels in 100 non-smokers working alongside active smokers. Again, the mean level was slightly up, 1.12%, but again the increase is hardly significant. Passive smoking, although undeniably unpleasant to some can hardly be described as a health hazard. The rise in COHb does not even approach that found in an

> active smoker. In the same City office we measured COHb in a 100 active smokers at the same time. They showed a mean level of 5.5% with a maximum of 13%, a completely different picture. We have rarely found a known non-smoker to exceed a level of 2.5% COHb and most are much lower. (p. 76)

Gori, G.B. and Mantel, N. (1991)[18]

> The daily levels of cigarette consumption compatible with no significantly increased risk for other diseases associated with active smoking appear to be of the same order as for lung cancer. Tables 4 and 5 report the analogous estimates for cardiovascular and respiratory disease mortality, with the implication that retained doses of ETS are unlikely to be associated with significant risk elevations for such disease as well. (p. 96)

Table 4 in the paper summarizes data from epidemiologic studies of smoking and heart disease, and provides the "maximum levels of daily cigarette consumption at which risk for coronary heart disease mortality in male smokers may not be significantly increased from the risk of nonsmokers." The maximum levels are in the range of 1.5-4.5 cigarettes per day. By contrast, Gori and Mantel calculate that the average ETS-exposure for a nonsmoker is "less than one cigarette over the course of 1 year."

> Together, these considerations suggest that the lung cell doses for average ETS-exposed nonsmokers are probably between 1/10,000 and 1/100,000 of equivalent cell doses for average mainstream active smokers. In practical

terms, this implies an annual retained dose of tobacco smoke components equivalent to far less than the dose from the active smoking of one cigarette somehow evenly dispersed over a 1-year period. (p. 94)

Malmfors, T., Thorburn, D. and Westlin, A. (1989)[19]

This is a study of the air quality in passenger aircraft, focusing on components related to ETS. Although no potential health effects were measured, the report emphasizes the low levels of ETS-related components, and observes these are unlikely to have an important cardiovascular significance. It is also noted that the nicotine and carbon monoxide levels in aircraft cabins are well below the standards set by OSHA.

It can be seen that the nicotine concentrations found in the present study are roughly one-tenth of the standard for the working environment set by OSHA. The concentration of carbon monoxide is also about one-tenth of the standard for general indoor air and even less for the working environment. (p. 623)

From this comparison it appears that the quality of the aircraft cabin air in the present study is satisfactory and better for factors related to ETS - nicotine and carbon monoxide - than for carbon dioxide and relative humidity. (p. 624)

Any effects on the cardiovascular system would have been mostly unnoticed in healthy individuals, because there are no known direct effects of ETS on the cardiovascular system beyond the formation of carboxyhemoglobin. The latter is so minimal that it will not affect the cardiovascular function. (p. 626)

Proctor, C.J., Warren, N.D., Bevan, M.A.J. and Baker-Rogers, J. (1991)[20]

> It seems that the main factor in exposure to environmental tobacco smoke is living with a smoker. Exposure at work, leisure, or travel seems to be minor. Overall, exposure to airborne nicotine was found to be low (mean 2.3 $\mu g\ m^{-3}$, median $<0.1\ mg\ m^{-3}$). (p. 296)

Mennear, J.H. (1993)[21]

> The role, if any, of environmental tobacco smoke (ETS) in the causation and/or exacerbation of cardiovascular disease remains to be proven and defined. . . . The findings show that there is scant clinical or experimental evidence to support a role for carbon monoxide in the causation of ischemic heart disease. Further, the results of field studies of relative air quality in nonsmoking and smoking homes, offices, and public places show that ETS contributes only minor and toxicologically insignificant increments in ambient carbon monoxide concentrations. These increments are variable and easily masked by other common carbon monoxide sources such as internal combustion engines and the burning of cooking and heating fuels. It is concluded that if ETS plays a role in the etiology of cardiovascular disease, it is most likely not mediated through carbon monoxide. (p. 77)

Roe, F.J.C., (1993)[22]

> Although it has not been proven that intermittent low peak levels of COHb do no permanent harm, it seems likely that the healthy body can compensate for them completely. (p. 120)

There is no clear evidence that exposure to CO is associated with an increased incidence of any form of cardiovascular disease. (p. 125)

Rylander, R. (1983)[23]

The unimportance of carbon monoxide has been further confirmed. . . . CO from ETS is not important from a health point of view. (p. 144)

Schievelbein, H. and Richter, F. (1984)[24]

Cardiovascular effects of tobacco smoke have been studied in passive smokers far less extensively than in active smokers. Under real-life conditions, passive smokers inhale approximately 0.02 to 0.01 of the amount of particulate matter taken up by active smokers. Their nicotine concentration in serum is within a range that is barely distinguishable from the background level. The increase in carboxyhemoglobin rarely exceed 1%. In healthy subjects heavily exposed to tobacco smoke, no or only slightly acute effects on the cardiovascular system are found. Whether or not passive smoking is likely to aggravate symptoms in patients with advanced coronary heart disease has not yet been unequivocally established and requires further investigation. From a few studies on occupational groups exposed to carbon monoxide (CO) and from experiments with animals chronically treated with CO or nicotine, the conclusion can be drawn that neither CO nor nicotine is likely to play a role in the development and progression of coronary heart disease in those concentrations normally found in passive smokers. (p. 626)

C. Literature emphasizing that any measurable acute cardiovascular responses to ETS are minor

(1) Healthy subjects

Several aspects of cardiovascular function, such as heart rate and blood pressure, can be readily measured in laboratory studies. Even if short-term changes in such parameters were consistently reported following acute exposure to ETS or CO, their potential clinical significance is highly uncertain. On the other hand, if the literature does not consistently report important acute cardiovascular responses, this further undermines claims of a potential relationship between ETS and heart disease.

A number of studies and reviews have examined potential acute cardiovascular responses to either ETS or CO. A sample of this literature is cited below, indicating a sizeable body of scientific data and opinion questioning a role of ETS or CO in such effects.

Committee on Passive Smoking, Board on Environmental Studies and Toxicology (1986)[25]

The report reviews studies of possible acute effects of ETS on the cardiovascular system in healthy subjects, and concludes that there are no significant changes. The report, although avoiding a firm conclusion, expresses that, for angina patients,

there is a possible cause for concern about exposure to the CO in ETS.

> In summary, for normal young adult males and females, no significant acute effects of ETS exposure on heart rate or blood pressure have been reported, either under resting or aerobic conditions. (p. 260)

Fischer, T., Weber, A. and Grandjean, E. (1978)[26]

Potential subjective, irritant and physiological (e.g., heart rate) effects of ETS were assessed in a laboratory setting. No pulmonary function or heart rate effects were reported. However, the authors nevertheless consider ETS a serious problem in view of irritant effects, potential effects in sensitive persons and levels to which some restaurant and bar employees are exposed.

> Pulmonary function tests should give us an indication of eventual bronchial constriction, encountered frequently in smokers. In fact, our spirometric methods showed no differences before and after exposure to smoke. The change in heart rate during the test was just as insignificant. (uncertified translation, p. 8)

Harke, H.-P. and Bleichert, A. (1972)[27]

> Measurements of electrocardiogram, blood pressure, and puls [sic] frequency showed, that these parameters were not altered by passive smoking. (p. 312)

Hulka, B.S. (1988)[28]

> Studies of acute ETS exposure in healthy children and adults have shown no statistically significant alterations in heart rate or blood pressure either during resting conditions or during exercise. Studies of ETS exposure in persons with pre-existing atherosclerotic heart disease have been inconclusive. Important questions about ETS exposure and the induction of angina, electrocardiographic abnormalities, and cardiac arrhythmias are unanswered. (p. 537)

International Collaborative Group (1984)[29]

This study examined children (approximately 13 years old) from cities in Germany, Cuba, Hungary and the USSR. Two sample groups were compared, one representing the upper 5% and one representing the remainder of the blood pressure distribution curve. One of the characteristics compared between these two groups was parental smoking habits. No significant association was reported between the children's blood pressure and parental smoking.

> The proportion of smokers among the fathers was slightly higher in the lower (55.8%) than in the upper group (54.7%); this difference was not significant. The proportion of smokers among mothers was, however, significantly higher in the lower than in the upper group ($P<0.01$). The proportion of smoking fathers was lowest in Berlin-Köpenick (46.3% vs. 38.6%) and highest in Havana (66.3% vs. 66.7%). The proportion of smoking mothers was lowest in Moscow 3 (0% vs. 1.4%) and highest in Budapest (29.4% vs. 32.0%). The mean blood pressure values of the children

showed no significant association with the smoking habits of either parent. (p. 122)

Pimm, P.E., R.J. Shephard and F. Silverman (1978)[30]

It is concluded that in normal subjects the magnitude of physiological responses to acute exposures is minimal. . . . (p. 201)

Rummel, R.M., Crawford, M. and Bruce, P. (1975)[31]

Heart rate and blood pressure measurements were made on 17 male and 39 female nonsmoking college students at 5, 10, 15, and 20 minutes during exposure to exhaled cigarette smoke in an enclosed room. . . . Measurements were correlated with attitudes toward smoke exposure.

For the entire group of nonsmokers, there were no significant changes in heart rate or diastolic blood pressure during the smoke exposure, but systolic blood pressure was significantly increased at 5 minutes of exposure; at 20 minutes of exposure it had returned to preexposure values.

When results were examined according to nonsmokers attitudes, those who "disliked" being exposed had significantly greater heart rates than those who were "indifferent" at all measurements; blood pressures between the two groups did not differ significantly.

Samet, J.M. (1988)[32]

> While these effects [relating to oxygen transport, heart and blood pressure increases, etc.] of carbon monoxide and nicotine may impair performance, exposures to environmental tobacco smoke are generally at concentrations below which physiological effects would be expected. (p. 12, col. 1)

Shephard, R.J., Collins, R. and Silverman, F. (1979)[33]

The responses of healthy men and women were measured during exercise performance while exposed to ETS vs. a sham exposure. Among several other variables, heart rate was measured. During a preexposure period, those subjects who were to undergo ETS exposure had higher heart rates than the sham subjects. However, actual exposure was associated with a smaller heart rate increase compared to the sham condition.

> The heart rate was higher before the experimental than before the sham exposures. . . . However, while actually exposed to the cigarette smoke both the increment of heart rate and the absolute heart rate were less than in the corresponding sham exposure. (p. 285)

The authors suggested that these heart rate changes might be related to a subjective anxiety or hyperventilation reaction, rather than an actual physiological response to ETS.

Turner, J.A.McM. and McNicol, M.W. (1993)[34]

In a partially blind randomized control study, nine healthy adult men performed progressive sub-maximal exercise tests, either after chewing nicotine chewing gun (4 mg) or breathing carbon monoxide (320 p.p.m.). Neither agent significantly affected exercise performance, despite a mean rise in blood nicotine to 17.0 ng ml^{-1} during nicotine administration and a COHb rise to 6.9% whilst breathing carbon monoxide. (p. 427)

Weber-Tschopp, A., Fischer, T. and Grandjean, E. (1976)[35]

Thirty three subjects were exposed in a climatic chamber to cigarette smoke (side stream) produced by a smoking machine. . . . $\%FEV_1/VC$, MMF and heart rate were not significantly affected during exposure. (p. 277)

Weber, A., Fischer, T. and Grandjean, E. (1979)[36]

In a first study subjects were exposed for 1 hr to constant cigarette smoke concentrations corresponding to 5 or 10 ppm CO. Annoyance, subjective eye irritations, and eye blink rate increase in both conditions during the first 30 min of exposure. Respiratory frequency and heart rate variability are not altered. (p. 205)

Winneke, G., Plischke, K., Roscovanu, A. and Schlipkoeter, H.-W. (1984)[37]

Neither blood pressure-values, nor heart-rates or fingerpulse-volume were influenced by exposure to tobacco-smoke. This correspond to the fact that nicotine-intake from passive smoking is negligible. Depth and rate of breathing were not altered either. (p. 353)

> As for carbon monoxide (CO) there was pronounced uptake in terms of COHb for the high exposure-condition only. In absolute terms, however, the measured values correspond to those found in non-smoking urban populations, and are well below levels considered critical for persons with cardio-vascular impairment. (p. 354)

Winneke, G., Neuf, M., Roscovanu, A. and Schlipköter, H.-W. (1990)[38]

Physiological measurements were obtained from nonsmokers, while they were in an exposure chamber in which another individual was smoking. No significant effects were reported for heart rate or blood pressure. The authors reported that "cardiorespiratory variables were not affected by ETS exposure." (p. 173)

> In taking CO as the basis for comparison our cardiovascular findings are consistent with those of others, who, at even higher levels of ETS-exposure did not observe exposure-related increase of either heart-rate or blood-pressure. Nicotine-intake at such ETS-levels is likely to be too low for cardiovascular changes to be expected. (p. 181)

(2) Angina and other heart disease patients

Claims are sometimes made that ETS, or specifically CO in ETS, aggravates cardiovascular disease in people with pre-existing illness. Such claims typically stem from a limited and largely discredited report by Wilbert Aronow that angina patients

experienced chest pain sooner when exercising in the presence of ETS.[39] However, a closer examination of the literature reveals a body of data that raises questions about whether ETS, or CO at levels reported to be in ETS, has significant adverse cardiovascular effects.

Hinderliter, A.L., Adams, K.F., Price, C.J., Herbst, M.C., Koch, G. and Sheps, D.S. (1989)[40]

> In conclusion, low-level CO exposure is not arrhythmogenic in patients with coronary heart disease and no ventricular ectopy at baseline. (p. 89)

McNicol, M.W. and Turner, McM. (1983)[41]

> There was no change in the mean oxygen uptake at the onset of angina with any intervention. . . . These results are in contrast with previous reports of the effects of smoking and carbon monoxide on exercise performance in angina pectoris. However in all of these other studies a subjective rather than objective end point was used. We suggest that an objective assessment is essential and that oxygen uptake at the onset of angina is useful and relatively easy to measure.

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Shephard, R.J., Collins, R. and Silverman, F. (1979)[42]

This study was an attempt to determine if asthmatic subjects have an increased sensitivity to ETS exposure. Respiratory symptoms, pulmonary function and heart rates were measured. Although some slight effects (e.g., a small heart rate increase) were reported, these were considered to be of "doubtful

biological importance" and most likely due to an emotional, rather than directly physiological, response to the ETS exposure.

> There was also some evidence of arousal and/or emotional excitement, including a slight tachycardia (at 80-min exposure, $P<0.05$) and a slight increase of forced vital capacity ($P<0.05$ at 90-min exposure). However, dynamic lung volumes . . . were unaltered. . . . Our data thus do not suggest that asthmatic subjects have an unusual sensitivity to cigarette smoke. (p. 392)
>
> The physiological changes observed in normal subjects during smoke exposure, although occasionally reaching conventional levels of statistical significance, were of doubtful biological importance (Pimm et al., 1978; Shephard et al., 1979a). Findings included some increase of heart rate and respiratory minute volume, probably of emotional origin, a tendency of increase in functional residual capacity and residual volume in some experiments, and small decreases of dynamic lung volumes. The asthmatic subjects also showed emotional reactions to the cigarette smoke, including the tachycardia, and possibly the preexposure increase of FRC and TLC. (pp. 399, 401)
>
> We would thus conclude that the specific sensitivity of asthmatic subjects is not a major consideration when determining air quality criteria for rooms contaminated by cigarette smoke. (p. 402)

Sheps, D.S., Adams, K.F., Bromberg, P.A., Goldstein, G.M., O'Neil, J.J., Horstman, D. and Koch, G. (1987)[43]

> In conclusion, there is no clinically significant effect of 3.8% COHb (representing a 2.2% increase from resting values) on the cardiovascular system in this study. (p. 108)

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SECTION VII

MATERIAL IMPAIRMENT: IRRITATION

IRRITATION

THE PROPOSED RULE DOES NOT CORRELATE COMPLAINTS OF IRRITATION WITH ACTUAL WORKPLACE EXPOSURES TO ETS, AND FAILS TO DEMONSTRATE THAT CURRENT ETS EXPOSURE LEVELS IN THE WORKPLACE POSE A SIGNIFICANT RISK OF MATERIAL IMPAIRMENT FROM "IRRITATION"

OSHA's Proposed Rule states that "mucus membrane irritation" is part of "a wide spectrum of health effects . . . associated with exposure to ETS." (59 FR 15973) In support of its claim that ETS is an "irritant," OSHA cites a single summary review of the literature (1986), two studies and six personal testimonials submitted to the RFI docket. (59 FR 15975) The Proposed Rule also lists several substances that have been defined as "irritants" by NIOSH and are reportedly found in tobacco smoke, but it concedes that specific constituents in ETS have not been directly related to irritation effects. (59 FR 15987-8, 15975)

The two studies on ETS and irritation cited in the Proposed Rule do not establish a significant risk of material impairment at current workplace exposure levels. The data in one of the studies cited in the Proposed Rule were collected in Switzerland in the late 1970s, and the high levels of respirable particulate matter reported therein are not relevant to current ETS exposure levels in the U.S. (Ex. 4-317) Moreover, the Proposed Rule does not address the authors' qualifications of the data in the study, i.e.,

> . . . there is a very poor correlation between the mean pollutant concentrations in each room and the corresponding results of the interview. This means that the measured pollutant concentration in an individual work room does not necessarily allow drawing conclusions on the extent of disturbance and irritations . . . .;
>
> Individual psychological factors (relationship with co-workers, work satisfaction, attitude toward smoking) considerably influence individual evaluation of disturbances and irritations . . . .;
>
> Thus, there is a considerable variance on the side of measurements of chemical and physical properties as well as on the side of subjective perception and feelings.

A second study cited in the Proposed Rule was conducted in Japan in the mid-1980s. (Ex. 4-18) Subjects were exposed to extremely high levels of tobacco smoke in an experimental chamber. The peak level of exposure to respirable particulate matter was nearly 100 times greater than levels encountered in workplace situations where smoking is permitted. The relevance of this experimental study to OSHA's claim about irritation is unclear; Benzene explicitly prohibits OSHA from basing its finding of "significant risk" at "lower levels of exposure . . . using evidence of health impairments at significantly higher levels of exposure." (AFL-CIO v. OSHA, 965 F.2d 962, at *978)

"Irritation" Defined

In the introduction to its standard governing workplace exposure to air pollutants, OSHA summarizes its authority as follows:

> Some impairments are so slight a discomfort that they are not material and do not provide a basis for regulation. A complaint of minor discomfort, in and of itself, is not material impairment. However, the OSHA Act is designed to be protective of workers and is to protect against impairment with less impact than severe impairment. (54 FR 2332, 1989)

OSHA also states:

> . . . [C]omplaints of minor irritation would not in and of itself constitute material impairment. In addition, OSHA would weigh irritation with physical manifestations more heavily than irritation with purely subjective responses. This does not mean that purely subjective responses would not constitute material impairment. That judgment would depend on the magnitude of the irritation. (54 FR 2362, 1989)

If OSHA is to support its claim that irritation from exposure to ETS is a material impairment, it must demonstrate that exposures bring about something more than subjective responses of minor irritation or annoyance, i.e., it must demonstrate the "magnitude" of the purported irritation effect. OSHA must demonstrate the "extent of the risk posed by individual substances," i.e., that existing exposure levels in the workplace

pose a significant risk of material impairment (due to irritation). It also must provide an "assessment of the level at which significant risk of harm is eliminated or substantially reduced." (AFL-CIO v. OSHA, 965 F.2d 962, 1992; *974, *979, *975)

OSHA will find little, if any, support for its position in the scientific literature. For instance, the major databases on sick-building syndrome indicate that tobacco smoke is rarely the underlying cause of complaints about irritation and annoyance related to indoor air quality. (Exs. 3-1053, 3-1073, 3-1074). ETS has been identified as a source of claimed discomfort in only two to five percent of a combined total of 1,000 sick-building investigations.[1-3]

Other published investigations of workplace venues report similar results. For example, in 1992, Canadian researchers reported results of a building investigation in which temperature, humidity, dust, nicotine, formaldehyde, volatile organic compounds, and CO_2 were measured.[4] Occupants of the building complained of poor indoor air quality, and a questionnaire evaluation revealed a substantial number of complaints about unsatisfactory thermal conditions, dry air, drowsiness and eye irritation. However, all measured parameters, including temperature and humidity, were within accepted comfort/exposure guidelines. The authors were unable to correlate any single measured environmental parameter

with complaints or symptoms. They concluded that their investigation "showed that complaints reported by occupants were associated with perceived rather than measured levels of indoor environmental parameters" [emphasis added].

A 1989 report by Hedge, et al. noted that while self-reported exposures to ETS were associated with increases in perceived symptoms of irritation, no significant correlations between actual levels of ETS constituents in the indoor air and symptom prevalence could be established. Moreover, the researchers reported that "passive smoking" was not associated with self-reports of mucus membrane irritation (MMI).[5]

Pimm and co-workers examined the effects of ETS exposures "at levels typically encountered in public buildings" in the late 1970s.[6] Physiological parameters such as lung flow rates, heart rates and blood carboxyhemoglobin levels were measured. The researchers reported that "the magnitude of the changes was small and of questionable biological significance." The authors also observed that "the subjects were also inevitably aware of the presence of the smoke, and the reported reactions may have been influenced by underlying beliefs and attitudes." Subjective complaints of irritation were categorized as "symptomatic" rather than physiological.

The Proposed Rule rejects the possibility that complaints about indoor air quality, and specifically complaints about ETS, may be mediated by a psychological component. The Proposed Rule suggests only that a "psychological overlay" may be common to complaints related to poor indoor air quality. (59 FR 15970) However, research indicates that the mere visibility or presence of ETS may provoke symptoms and complaints.[7,8] Winneke and colleagues found that aversion to ETS increased the degree of annoyance and irritation reported under experimental exposure conditions.[7] Researchers from the Illinois Institute of Technology in 1992 reported that simple visual contact "with a source of tobacco odors" increased both perceived odor intensity and the number of subjects perceiving tobacco odor.[8]

Other recently published studies have demonstrated the importance of variables such as job stress, including work control, support, possibilities for personal growth and job satisfaction, in the perception of symptoms due to sick-building syndrome.[9,10] The studies suggest that such factors may either be directly related to symptoms as stress reactions, or they may play a role in rendering the individual more prone to react to environmental influences, including perceived exposures to ETS.[9,10]

ETS is easily identified and is often blamed as the cause of complaints of annoyance and irritation, especially among

individuals who dislike tobacco smoke. However, a workplace that is adequately ventilated with outdoor air effectively addresses and prevents complaints of irritation and annoyance, regardless of the suggested source.[1-3] ASHRAE ventilation Standard 62-1989 was developed in order to minimize potential complaints of annoyance and irritation in indoor environments. The ventilation rates in the Standard specifically address ETS. The Standard's design criteria currently apply to buildings that have been constructed, renovated or remodeled in the U.S. after 1990. Indeed, the Standard is incorporated by reference into OSHA's Proposed Rule on IAQ. (59 FR 16036)

OSHA's Proposed Rule calls for the complete elimination of ETS exposure in the workplace. This proposal, of course, will not eliminate exposure to irritants in the workplace, since precisely the same irritants imputed to tobacco smoke by OSHA are emitted from other sources. (59 FR 15987-8, 15984) Specific irritants reported in tobacco smoke and generated as well from other indoor sources include formaldehyde and other volatile organic compounds such as acetaldehyde, acrolein, etc. 59 FR 15987-8)

The levels of "irritants" found in the indoor air of the nonindustrial workplace typically overwhelm any possible contributions from tobacco smoke. For example, Godish, in his

review of formaldehyde exposures from tobacco smoke, writes that even under "extreme circumstances, the effect of cigarette smoking on formaldehyde levels in indoor spaces would be negligible.[11] Guerin, et al., similarly conclude that "as such, it has been difficult for many studies to demonstrate consistently elevated levels of formaldehyde due to ETS."[12] (Ex. 8-129, also submitted to OSHA as Ex. 3-499) They also conclude: "Studies of offices, restaurants, train compartments, and public buildings suggest that ETS contributes to the indoor air burden of VOCs but that other sources predominate. Major sources include building materials, furnishings, cleaning products, office machines, gasoline, and combustion sources associated with cooling, heating, and transportation."[12] Clearly, these results indicate that contributions from ETS to ambient levels of "irritants" are minimal and often indistinguishable from background levels. Any potential risk from irritation associated with ETS therefore would be addressed with the implementation of OSHA's own Proposed Rule on indoor air quality (a ventilation-based indoor air quality standard).

The scientific record is devoid of any data suggesting that ETS is an irritant under current workplace exposure levels and/or under conditions of adequate ventilation (e.g., outdoor air rates specified in ASHRAE 62-1989). OSHA's proposal to reduce alleged irritation from ETS through the complete elimination of

smoking in the workplace is equivalent to the "regulation of insignificant risks." Benzene clearly states that reduction of significant risk is not tantamount to elimination of all "risk," but only the level or range that may be deemed "significant." (IUD v. API, 448 U.S. 649-651) OSHA has failed to determine any level of that purported "risk."

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SECTION VIII

MATERIAL IMPAIRMENT: PULMONARY EFFECTS

PULMONARY EFFECTS

OSHA DOES NOT EXERCISE ANY CONSISTENCY OR PURPOSE IN ITS CITING OF THE PUBLISHED LITERATURE; STUDIES ARE CITED FOR IRRELEVANT OR MINOR POINTS, WHILE PERTINENT DATA FROM THE STUDIES ARE NOT REPORTED OR DISCUSSED; OSHA DOES NOT PRESENT ANY CONCRETE ARGUMENTS TO SUPPORT THEIR CONTENTIONS

This is a consistent problem throughout this section of OSHA's Proposed Rule on IAQ/ETS. It appears as though OSHA chooses irrelevant points from studies so as to be able to reference them, while the pertinent data from the studies are ignored in the discussion. No critical analysis is presented, and OSHA makes no concrete arguments to support its conclusion that there is an association between exposure to ETS in the workplace and pulmonary effects in nonsmokers.

OSHA presents data which are irrelevant to a discussion of potential pulmonary effects in nonsmokers exposed to environmental tobacco smoke in the workplace

OSHA's task is to show that there is a significant risk of material health impairment in nonsmokers exposed to environmental tobacco smoke in the workplace. OSHA, however, bases its "review" of pulmonary effects on one experimental study (Ex. 8-18) in humans as well as on several epidemiological studies (Exs. 8-37, 8-62, 8-148, 8-173, 8-176, 8-178, 8-180, 8-209, 8-210, 8-278, 8-

295, and 8-321), most of which examined reported exposures to ETS in the home environment. OSHA also discusses several animal inhalation studies. (Exs. 8-322, 8-204, 8-290, 8-104, 8-45, and 8-114) OSHA concludes the following:

> The weight of the evidence shows that exposure to ETS results in decreases in pulmonary function indices and increases in respiratory symptoms in otherwise healthy men and women who are exposed to ETS for periods of 10 or more years. [emphasis added] (59 FR 15977)

Because there are studies available that have examined potential effects of exposure to ETS on the respiratory health of nonsmoking adults in the workplace, those are the studies which should be reviewed and analyzed in this section. OSHA presents no critical discussion of the data available from these studies and makes no scientifically supportable claims regarding causation. Recent reviewers of the pulmonary effects literature (who are affiliated with the International Agency for Research on Cancer) concluded that "on the basis of the available data, no definite conclusion (excluding the acute irritating effect of ETS on respiratory mucous membranes) can be drawn."[1] The reviewers' conclusions were not discussed in the Proposed Rule.

OSHA relies on an experimental exposure chamber study which did not examine or make any conclusions regarding respiratory endpoints in nonsmokers exposed to ETS

OSHA cites a 1983 study by Asano, et al. (Ex. 8-18) This study was an experimental exposure chamber study of only 20 subjects, including 5 male smokers, 5 male nonsmokers and 10 female nonsmokers. It is unclear why OSHA included this study in the pulmonary effects section, since the study reports on non-pulmonary endpoints such as systolic blood pressure and heart rate. This study is therefore irrelevant to a discussion of potential pulmonary effects in nonsmokers exposed to ETS in the workplace.

OSHA RELIES ON SURVEY REPORTS OF NONSMOKERS WHO LIVE WITH ONE OR MORE SMOKER(S); THESE STUDIES SUFFER FROM IMPORTANT FLAWS, AND DO NOT CONSTITUTE THE "BEST AVAILABLE EVIDENCE" REGARDING POTENTIAL PULMONARY EFFECTS IN NONSMOKERS EXPOSED TO ETS IN THE WORKPLACE

The epidemiological literature upon which OSHA bases its conclusion suffers from a couple of very important problems. First, very few of the studies report on workplace exposures to environmental tobacco smoke, the very issue OSHA is proposing to regulate. Second, the studies contain no actual exposure data. In the majority of studies, the estimation of exposure originates from questionnaire responses of subjects and/or their spouses and co-habitants. Even though the studies suffer from these problems, the magnitude of the reported decrements in pulmonary function in

healthy nonsmokers reportedly exposed to environmental tobacco smoke, as OSHA itself concedes, is very small and of questionable biological or clinical significance.

Among the epidemiologic studies OSHA chose to rely on are several studies of reported home exposures to ETS. The 1985 study by Brunekreef, et al. estimated exposure of nonsmoking women in the Netherlands by asking the subjects to quantify the number of cigarettes smoked daily inside the home by household members. While this study, on cross-sectional analysis, reported that several pulmonary function parameters appeared to be significantly associated with exposure to ETS in the home while others did not, the authors also reported that "there was no association between [ETS] exposure and pulmonary function decline." (Ex. 8-37)

Another study referenced by OSHA, a 1981 paper by Comstock et al., examined reported home exposures of 1,724 adults to environmental tobacco smoke. (Ex. 8-62) The authors of this study, epidemiologists at the Johns Hopkins University School of Medicine, reported:

> The presence of a smoker in the household other than the subject <u>was not associated with the frequency of respiratory symptoms, and only suggestively associated with evidence of impaired ventilatory function</u>. [emphasis added]

A 1989 study by Hole, et al., is also cited by OSHA. (Ex. 8-148) In this paper, "passive smoking" was defined as living at the same address as a smoker. Additional attempts to quantify exposure involved questioning subjects regarding the number of cigarettes smoked daily by their co-habitee. While this study reported associations between living with a smoker (as a surrogate of ETS exposure) and several respiratory health endpoints in nonsmokers, the 95% confidence interval fell below unity for all respiratory endpoints (i.e., the associations were not statistically significant).

In the Letter to the Editor written by Kalandidi in 1987, which informally reports on a study the author was conducting in Greece that suggested exposure to environmental tobacco smoke "may contribute to the cause of COLD [chronic obstructive lung disease]," the author writes that the studies on exposure to ETS and adult respiratory health contain data that are "equivocal." (Ex. 8-173) In 1990, Kalandidi reported these data in a published paper.[2] While the data were suggestive of a possible association, it is questionable whether the authors adequately considered other potential exposures which have been associated with the development of COLD such as the extremely high levels of outdoor air pollution found in Greece.

OSHA cites two studies by Kauffman, et al. The first study, published in 1983, reports on home exposures to ETS of nonsmoking women married to smokers. (Ex. 8-176) The second study, published in 1989, reports on similar data. (Ex. 8-178) While the authors reported an association between decreased lung function and "passive smoking" in French women, the authors reported that "no significant association between passive smoking and level of lung function" was apparent in American women. Dr. Michael Lebowitz (a member of the EPA's Science Advisory Board Committee which reviewed the EPA's Risk Assessment on ETS) has questioned the conclusions of the Kauffman study (Ex. 8-176), which, as mentioned above, reported significant differences in lung function between exposed and nonexposed nonsmokers in one part of the study population but no significant differences in the population as a whole. Dr. Lebowitz noted that since the "healthiest" part of the study population lived in the most polluted areas, the study may have been flawed due to biased population selection and testing for other confounding factors.[3]

Since OSHA decided to rely on epidemiologic studies of reported ETS exposures in the home, studies of reported home exposures not cited by OSHA in its proposed rulemaking warrant mention.[4-6] In 1983, for example, Jones, et al., reported that in a case-control study of several hundred nonsmoking women from a U.S. study population, there was no significant association between

decreases in lung function and exposure to ETS in the home.[4] Similarly, Lebowitz, et al., coordinators of an epidemiologic study of obstructive lung disease in Arizona, reported no association between reported ETS exposures in the home and respiratory health in their adult study population.[5] In a study of 376 families, Yale University scientists Schilling, et al., also reported no evidence that environmental tobacco smoke affects either lung function or respiratory symptoms in adults.[6]

Similarly, OSHA failed to discuss various government reviews of the ETS and adult respiratory health literature which have generally concluded that there is a negligible association, <u>if any</u>, between exposure to ETS and respiratory health effects in adult nonsmokers. For example, the 1986 Surgeon General's report on ETS concluded:

> Healthy adults exposed to environmental tobacco smoke may have small changes on pulmonary function testing, but are unlikely to experience clinically significant deficits in pulmonary function as a result of exposure to environmental tobacco smoke alone.

Other researchers who have analyzed these reported data contend that the results are "mixed and inconclusive." For example, researchers in France, Laurent, et al., have commented that purported long-term health effects from exposure to ETS are difficult to demonstrate in healthy adults and that the results of

the epidemiological studies are "sometimes conflicting and often open to question."[7] One investigator who is critical of ETS conceded that "the effect of passive smoking on respiratory infections in adults has not been well characterized and reports of its effects on chronic respiratory disease in adults have been inconsistent."[8]

In his summary of the studies on respiratory symptoms and diseases in adults published up to early 1990, American investigator Dr. Philip Witorsch noted that while "4 of 8 [reported] an increased frequency, 4 of 8 [reported] no increased frequency." He stated that, in addition to "all of the problems" with the studies, "these results are too variable to permit any conclusion of association."[9] As his summary demonstrates, the conclusion of the participants at the 1983 U.S. National Institutes of Health workshop on ETS exposure, that the possible effect from ETS "varies from negligible to quite small," is still pertinent.[10]

Thus, OSHA's Proposed Rule has not demonstrated a significant risk of material impairment to health associated with possible pulmonary effects in nonsmokers exposed to ETS in the workplace. Both the literature cited by OSHA and additional material omitted from the Proposed Rule report data which are equivocal and which appear to lack clinical significance.

THE EPIDEMIOLOGIC STUDIES WHICH EXAMINED REPORTED WORKPLACE EXPOSURES TO ETS IN NONSMOKING ADULTS HAVE REPORTED INCONSISTENT AND INCONCLUSIVE DATA; THE STUDY UPON WHICH OSHA PLACES THE MOST WEIGHT HAS RECEIVED SUBSTANTIAL CRITICISM IN THE SCIENTIFIC LITERATURE FOR QUESTIONABLE DATA ACQUISITION AND ANALYSIS; OSHA FAILS TO ADDRESS ANY OF THESE CRITICISMS

OSHA reports on four studies which contain discussions of workplace exposures to environmental tobacco smoke. Probably the most familiar study mentioned in this section is the 1980 White and Froeb study. (Ex. 8-321) While this study is often cited by individuals in support of an association between exposure to environmental tobacco smoke in the workplace and small airways dysfunction in healthy nonsmokers, the study has received substantial criticism in the published literature. OSHA does not address any of these criticisms in its Proposed Rulemaking.

In regard to the White and Froeb study, a physician at a U.S. medical school questioned their use of carbon monoxide as an index of smoke exposure, contending that they "do not have reliable estimates of the smoke exposure in the environment of their nonsmokers" because it is not unique to tobacco smoke.[11] A British reviewer shared the physician's view that White & Froeb's findings "relate to an index which is contentious and certainly not an accepted reliable indicator of an increased health risk."[12] White and Froeb themselves noted that the average values of the pulmonary

tests of nonsmokers exposed to tobacco smoke "were not notably different" from the values suggested as normal by a specialist in this area.[13]

Perhaps the most telling criticisms of the study were voiced by Dr. Michael Lebowitz of the University of Arizona at an annual joint meeting of the American Lung Association/American Thoracic Society and in a subsequent letter published in the U.S. Congressional Record.[14-15] During a forum at the ALA meeting, Dr. Lebowitz stated that he had concluded, from his own extensive review of the study and from an interview with White, that the study was "improperly designed" from an epidemiological point of view. He noted that there were problems "inherent" in the study, including the selection of the study group and the measurement of smoke in the workplace. Dr. Lebowitz also expressed concern that the statistical significance of the data appeared to depend on the unexplained omission of data for 3,000 people who were originally included in the study. Based upon these considerations, Dr. Lebowitz urged that the study not be used to support the claim that exposure to ETS in the workplace affects the lung function of healthy nonsmoking adults.

Dr. Lebowitz again took issue with the White and Froeb study in a 1984 paper he presented at the Vienna Symposium on Passive Smoking.[3] He contended:

> Even with a biased population, poor study design, and incorrect statistical evaluation, there were no clear-cut, consistent, medically meaningful differences between passive smokers and groups of nonsmokers; a corrected statistical analysis strengthened this conclusion.

Fielding and Phenow, whose conclusion that the "changes" reported by White and Froeb were "equivalent to those found in light smokers, who smoke from 1 to 10 cigarettes per day" is reported by OSHA, also made several highly relevant statements that are not mentioned by OSHA. (Ex. 8-102) Fielding and Phenow suggest that the data from the studies on ETS exposure and adults "have been conflicting" and that "taken together, the limited data on the effect of [environmental tobacco] smoke on adult lung function are inconsistent and inconclusive."

In addition to these concerns, the data from the White and Froeb study appear to be inconsistent with other data on lung disease and lung function in nonsmokers. For example, a 1984 study of 1,351 German office workers by Kentner et al., reportedly found no effect of ETS on pulmonary function among exposed nonsmokers. (Ex. 8-180) In a 1988 update of the study, the investigators noted that "there is no evidence that average everyday passive smoke exposure in the office or home leads to an essential reduction of lung function in healthy adults." The key investigator reiterated these conclusions in 1989 and 1990 publications. The 1984 study is

cited by OSHA in its proposed rule, but no discussion of the study or its data is included.

Two other studies cited by OSHA which report data on workplace exposures of nonsmoking adults to ETS suffer from serious problems regarding exposure assessment. The Masi (1988) study reported on 293 subjects, aged 15 to 35 years old. (Ex. 8-209) The study, however, contains such crude "exposure" data that it is disturbing that OSHA deems it reliable. Workplace "exposure" to ETS was assessed in the following manner:

> Bank employees were asked to [subjectively] assess smoke conditions in the work area as light, moderate, heavy or unable to quantify. . .[these categories] were arbitrarily converted to number of cigarettes. [emphasis added]

Similarly, the authors of the Masjedi (1990) study conceded that most of their subjects "were unable to quantify the amount of [their] exposure to passive smoke. . ." (Ex. 8-210)

THE EPIDEMIOLOGIC AND EXPERIMENTAL DATA AVAILABLE DO NOT SUPPORT OSHA'S CONTENTION THAT COMPROMISED INDIVIDUALS IN THE WORKPLACE HAVE A SIGNIFICANT RISK OF MATERIAL HEALTH IMPAIRMENT BECAUSE OF EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE

OSHA claims that although the pulmonary function decrements reported to be associated with exposure to ETS in

healthy nonsmokers are small and of questionable clinical significance, these changes may become significant in persons with already impaired pulmonary function (e.g., asthmatics). In its attempt to substantiate this claim, OSHA references two experimental studies on adult asthmatics exposed to ETS for one hour in an exposure chamber. The first study, Knight and Breslin, 1985, reported on only six subjects, four of whom had previously given a positive history of ETS "attacks." (Ex. 8-182) The authors (and OSHA) did not discuss the possibility that psychological factors may have played a role in the subjects' reported "reactions" to the ETS exposure.

The second study, by Dahms et al., 1981, reported on ten patients with asthma (five of whom were included because they reported specific complaints when exposed to cigarette smoke) and ten normal patients. (Ex. 8-76) While the authors reported an association between exposure to ETS and lung function responses in the asthmatic subjects, they reported that "not all subjects showed the same pattern of pulmonary responses to the smoke exposure." The authors also reported that "we were not able to exclude the possibility that these changes in pulmonary function were emotionally related to cigarette smoke" [emphasis added]. Similarly, the 1986 Surgeon General's report recognized that "in this study, subjects were not blinded as to the exposure and were selected because of complaints about smoke sensitivity."

OSHA also references a 1991 review article by Stanton Glantz and Richard Daynard (Tobacco Liability Project) which makes several claims regarding exposure to environmental tobacco smoke, none of which is supported by a thorough and critical review of the scientific literature available. (Ex. 3-438D)

OSHA claims that asthmatics are believed to be especially sensitive to various environmental influences, including ETS, but a thorough review of the scientific data on ETS does not convincingly support this contention. There are currently ten major studies on ETS exposures among adult asthmatics. Seven of the studies are clinical in nature, where exposures to ETS were controlled under laboratory conditions. The other three studies are population surveys. All of the studies evaluate reports of respiratory symptoms such as coughing, wheezing, and irritation ("subjective complaints") and changes in lung function (an "objective" test for lung impairment).

Only two of the seven clinical studies report objective decreases in lung function among the majority of asthmatics exposed to environmental tobacco smoke. However, the patients in both positive studies were exposed to excessively high and unrealistic levels of ETS [15-32 ppm carbon monoxide], and, as mentioned above, the authors of one of the studies conceded that the observed effects may have been due to psychological factors. In the

remaining five clinical studies, a number of patients reportedly complained of subjective symptoms upon exposure to ETS, but objective results (i.e., evidence of airways obstruction or significant changes in lung flow rates) were not observed in the vast majority of patients.[16-20]

Data from the three population surveys on adult asthmatics are generally consistent with data reported in the majority of clinical studies.[21-23] A report of a large-scale population survey in the U.S. suggested that ETS exposures in the home did not affect either symptoms or pulmonary function in adult asthmatics. Another group of U.S. researchers recently reported that exposure to ETS did not impair lung function in the 263 asthmatic adult subjects studied. The third study reported mixed results for the development of asthma-related symptoms in individuals reporting exposures to ETS during childhood and adulthood.

OSHA FAILS TO DISCUSS THE PROBLEMS IN GENERALIZING DATA FROM "EXPOSURE CHAMBER" STUDIES TO THE "REAL-WORLD" SITUATION

As mentioned above, the conditions under which asthmatic patients are exposed to ETS in these studies are of questionable relevance to "real-life" exposures. The Surgeon General, in the

1986 report on ETS, conceded that exposure chamber studies may not be indicative of the "real world" situation:

> Acute exposure in a chamber may not adequately represent exposure in the general environment. Biases in observation and the in [sic] selection of subjects and the subjects' own expectations may account for the widely divergent results. Studies of large numbers of individuals with measurement of the relevant physiologic and exposure parameters will be necessary to adequately address the effects of environmental tobacco smoke exposure on asthmatics.

THE MAJORITY OF ANIMAL STUDIES REFERENCED BY OSHA ARE STUDIES OF MAINSTREAM TOBACCO SMOKE AND ARE NOT RELEVANT TO A DISCUSSION OF POTENTIAL PULMONARY EFFECTS IN NONSMOKING ADULTS EXPOSED TO ENVIRONMENTAL TOBACCO SMOKE IN THE WORKPLACE

Although OSHA refers to the studies in this section as experimental "ETS" studies, the majority of the studies are mainstream smoke studies which have little or no relevance to ETS issues. ETS is not the same as either mainstream or sidestream smoke. For a complete discussion of this issue, please refer to the section on exposure issues in this submission.

OSHA mentions isolated conclusions from several experimental animal studies but makes no attempt to explain how these data relate to real-life ETS exposures of nonsmoking adults in the workplace. OSHA also does not make any attempt to explain

the physiological or clinical significance, if any, of the reported data. Nor does OSHA address the apparent inconsistencies in the reported data. For example, "effects" may be reported in one species but not in another.

OSHA makes no attempt to explain the relevance, if any, of these high-dose experiments in animals to real-life workplace exposures in humans, even when some of the studies from which they report data acknowledge that these exposure levels are extreme when compared to the "real world" of "smoke-filled" restaurants or offices. OSHA's responsibility in this proposed rulemaking is to show that workplace exposures to ETS are likely to result in material health impairment in non-smoking adults. They have failed to substantiate this claim.

OSHA FAILS TO REFERENCE MUCH OF THE RELEVANT LITERATURE SUBMITTED IN RESPONSE TO THE OSHA RFI IN 1992

OSHA presents no critical discussion of potential confounding factors, merely stating that the studies "varied" in their consideration of such factors and that "several studies" have examined isolated variables; OSHA makes no statement regarding the adequacy of control for such factors in these studies

In the Proposed Rule, OSHA presents selected data on the possible association between exposure to ETS and decreased pulmonary function in adult nonsmokers. Philip Morris submitted much of the literature which OSHA has omitted from its Proposed Rule to the docket for the RFI in 1992. (Ex. 3-1074) For a discussion of this literature, please see the response to question 2(a)iii in Ex. 3-1074. A discussion of confounding factors, which OSHA does not provide in its Proposed Rule, is also presented in that section of Ex. 3-1074.

OSHA, while conceding that the studies on ETS exposure and pulmonary effects in nonsmoking adults "vary by numerous factors," makes no apparent attempt to explain why these variations are given no importance in their "analysis" of the literature

OSHA does not elaborate on its statement that the studies on ETS exposure and respiratory effects in nonsmoking adults "vary by numerous factors, such as the population studied, the measures

used to estimate exposure to ETS, and the physiologic and health outcomes examined." While other reviewers of this body of literature have concluded that it is difficult, if not impossible, to make any definitive conclusions from these data, OSHA attempts, but fails, to make a case for causation.

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SECTION IX

MATERIAL IMPAIRMENT: REPRODUCTIVE EFFECTS

REPRODUCTIVE EFFECTS

OSHA'S PROPOSED RULE LACKS CONSISTENCY IN ITS DEFINITION OF "ETS EXPOSURE DURING PREGNANCY"

In some instances, OSHA appears to be discussing the potential effects on the fetus that may be associated with active smoking of the mother during pregnancy. At other times, the authors of the Proposed Rule are discussing ETS exposure of the mother during pregnancy. Active smoking of the mother during pregnancy is not synonymous with ETS exposure. OSHA's task is to show that there is a significant risk of material health impairment in fetuses whose mothers are exposed to ETS at work during their pregnancies. The studies referenced by OSHA which examine active smoking during pregnancy are irrelevant to this discussion.

The majority of the studies OSHA references in this section are irrelevant because they deal with active smoking of the mother during pregnancy, not ETS exposure of the mother during pregnancy; ETS and mainstream tobacco smoke are not equivalent

A detailed discussion of the differences between ETS, sidestream and mainstream tobacco smoke is provided in exposure section of this submission.

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OSHA provides a brief, selective and seemingly irrelevant discussion regarding the possible association between workplace ETS exposures of nonsmoking pregnant women and various adverse reproductive outcomes

OSHA claims that "other reproductive effects that have been ascribed to maternal ETS exposure include miscarriage, an increase in congenital abnormalities, and numerous other physiological effects." (59 FR 15979) As references for this section, OSHA provides citations to the Taylor and Wadsworth (1987) study. (Ex. 8-299) This study examined active maternal smoking and reported no data on ETS exposures during pregnancy. OSHA also cites a response to a Letter to the Editor by Ira Tager. (Ex. 8-297) In this letter, Tager makes no mention of "other physiological effects" in infants born to mothers reportedly exposed to ETS during pregnancy and states the following regarding this issue:

> In discussing the harmful effects of passive smoking [during pregnancy], it is important to point out that there is no body of data that absolutely proves that harmful effects will be experienced.

OSHA also claims that "the effects of environmental [tobacco] smoke exposure on the fetus may have long-term sequelae into childhood and adulthood." (59 FR 15979) The first three studies cited by OSHA make no mention of any purported "effects" of

ETS exposure during pregnancy on the fetus. (Exs. 8-53, 8-181, 8-213) The fourth study cited by OSHA is a study of active maternal smoking during pregnancy. (Ex. 8-225) OSHA also references a CDC survey which provides no information, conclusions, or data regarding the possible effects of maternal ETS exposure during pregnancy. (Ex. 8-51) Finally, OSHA again cites the response to the Letter to the Editor by Ira Tager outlined above. (Ex. 8-297)

OSHA states that exposure to ETS may be "reflected in the growing child as reductions in lung development" and that "this is especially relevant if that child continues to be exposed to ETS throughout childhood and into adulthood." (59 FR 15979) OSHA again references the Tager letter above to support this point. (Ex. 8-297) It also cites a paper which reports:

> Paternal smoking does not appear to be the environmental exposure leading to both childhood respiratory illness and adult chronic air-flow limitation. [emphasis added] (Ex. 8-177)

OSHA DOES NOT PROVIDE A BALANCED AND COMPLETE DISCUSSION OF THE LITERATURE AVAILABLE, I.E., OSHA FAILS TO MENTION STUDIES WHICH REPORT NO ASSOCIATION BETWEEN EXPOSURE TO ETS DURING PREGNANCY AND ADVERSE REPRODUCTIVE OUTCOMES

In 1992, one group of researchers examined the issue of maternal ETS exposure during pregnancy and spontaneous abortion

(miscarriage).[1] Although the authors reported that paternal smoking was not associated with spontaneous abortion (after consideration of other independent risk factors), exposure to ETS from sources other than the father was reportedly associated with an increased risk of miscarriage. This is surprising considering that fact that the authors observed no excess risk of spontaneous abortion among "moderate" smoking mothers or among those who actively smoked an average of more than 20 cigarettes per day in the first trimester. The inconsistent and contradictory data from this study appear to be the result of inadequate control for other factors.

Other research has suggested possible associations between maternal exposure to ETS during pregnancy and infant size, premature labor and neonatal asphyxia.[2] In contrast, Savitz, et al., reported that they could provide "no definitive evidence" of an association between paternal smoking and any birth defect.[3] Other authors similarly have reported no associations between maternal exposure to ETS during pregnancy and the incidence of heart defects,[4-5] premature rupture of amniotic membranes,[6] strabismus (an eye disorder)[7] and various other birth defects.[8]

Although several isolated studies have suggested an association between reported exposures to ETS during pregnancy and various conditions in the infant, the data must be considered both

inconclusive and, in the words of one scientist, "controversial."[9] Another author has suggested:

> Much remains to be done in order to determine whether ETS has any effect on human reproduction or development. Improvements in design of epidemiologic studies of ETS effects, particularly in the areas of exposure assessment and validation and elimination of confounders, are especially important. In addition, appropriate animal studies would be helpful in allowing definitive conclusions to be drawn.[10]

DESPITE THE IRRELEVANCE OF MUCH OF THE LITERATURE OSHA CITES, OSHA STILL FAILS TO PROVIDE A CRITICAL DISCUSSION OF THE PROBLEMS INHERENT IN SUCH EPIDEMIOLOGICAL STUDIES

Probably the most important problems in epidemiologic studies are the lack of quantitative exposure data and the lack of adequate control for potential confounding factors. Exposure estimates in these studies are based on questionnaire information, the validity of which have been questioned repeatedly in the scientific literature.[10] OSHA conveys the impression that confounding factors have been adequately ruled out in these studies. OSHA fails to mention data which, after being adjusted for other factors, have failed to reach statistical significance. The control of confounding variables is of extreme importance in ETS studies examining birth weight. ETS exposure has been shown to "correlate positively with a number of known determinants of

decreased birth weight," including lower socioeconomic status and poor nutrition.[10] Another group of authors suggests that "it is generally believed that birth weight, perinatal mortality and other measures of reproductive health are sensitive markers of social conditions."[11]

OSHA claims that confounding factors have been adequately ruled out as an explanation for the reported association between paternal smoking and reductions in infant birthweight. OSHA mistakenly arrives at this conclusion by taking factors that were controlled for in a few of the studies and generalizing to the entire population of studies.

In addition to these general problems, there are problems specific to the studies OSHA chose to cite in its Proposed Rule. For example, to support its statement that "data on the reproductive effects due to the exposure of nonsmoking pregnant women to ETS has been presented in many studies," OSHA references two abstracts and six papers. (Exs. 3-438, 8-92, 8-174, 8-208, 8-273, 8-285, 8-287, 8-299) A complete review of the statistical procedures and methods, let alone the data, cannot be performed on abstracts.

There are also problems specific to several of the papers cited by OSHA. For example, the Martin & Bracken paper reported

that women who were reportedly exposed to someone else's cigarette smoke for at least two hours per day, either at home or at work, during pregnancy delivered infants that were, on average, 24 grams lighter than the infants of women who were reportedly not exposed to ETS. (Ex. 8-208) This relationship was not statistically significant. This paper is also used to provide support for OSHA's statement that "passive exposure to tobacco smoke is estimated to double the risk of low birthweight in a full-term baby." (59 FR 15979) While the authors reported a relative risk of 2.7 (95% confidence interval 1.05-4.50) for a subgroup of the women, when all women with full-term deliveries were included in the analysis there was no statistically significant relationship between reported exposure to ETS during pregnancy and a reduction in infant birthweight. As one author wrote in 1990:

> The analyses reported by Martin and Bracken (1986) are inconsistent and difficult to interpret. This may be due, at least in part, to the authors' use of a relatively crude estimate of ETS exposure. Their findings would have been more meaningful if further information had been available regarding exposure intensity and duration. Further, since questionnaire data were solicited early in gestation, intensity and duration of ETS exposure may have changed considerably for a number of subjects over the remainder of pregnancy.
>
> Potentially important confounders, such as maternal weight and the child's sex, were apparently not determined during the data collection, and thus were unavailable for the

> analysis, although such variables may significantly influence birth weight.
>
> It is puzzling that the authors used statistical significance as the criterion for inclusion of potential confounders in their multiple regression analyses when, according to various experts, this may eliminate important confounders (e.g., because of low statistical power or multicollinearity).[10]

It should not, then, be surprising that Martin and Bracken conceded that "whether the association found [between decreased infant birthweight and ETS exposure during pregnancy] is due to passive smoking or to some other related factor is unclear" [emphasis added].

The Rubin (1986) paper reported that each pack of cigarettes smoked by the father each day during a mother's pregnancy was associated with a 120 gram reduction in the offspring's birthweight. (Ex. 8-273) However, even a reviewer who is critical of parental smoking, Trichopoulos, has stated that the reported reduction in birthweight reported by Rubin was "extraordinarily large" probably because of poor control for confounding factors.[12] Similarly, another author wrote the following regarding the 1986 Rubin paper:

> An ETS effect of this relative magnitude seems improbable, however, when the relative degrees of exposure are considered. Moreover, in their regression analysis of paternal smoking effects, the authors failed to include interaction terms. This is true even though

> they reported finding a significant interaction between social class and paternal smoking effects, and earlier studies had reported interactions between effects associated with maternal and paternal smoking status. Rubin and coworkers failed to control for a number of other potential confounders as well.[10]

A study which reports the following is also cited by OSHA:

> We report negative results on induction of chromosomal damage in 2 separate groups of intensive involuntary exposure to tobacco smoke, non-smoking restaurant personnel and newborn children of smoking mothers. (Ex. 8-287) [emphasis added]

Finally, the other study cited by OSHA is a paper on the possible effects of active smoking by the mother during pregnancy. (Ex. 8-299) The paper contains no data on pregnant mothers who are exposed to ETS in the workplace during pregnancy.

OSHA fails to discuss a number of other studies which have reported no statistically significant associations between maternal exposure to ETS during pregnancy and the delivery of low birthweight infants.[13-19] In fact, one study considered 57 different risk factors for low birthweight infants and reported that paternal smoking (as an index of exposure to ETS) had no statistically significant effect on infant birth-weight.[13]

OSHA does not provide a detailed discussion of the clinical significance, if any, of the reported decrements in infant birthweight allegedly associated with ETS exposure of the mother during pregnancy.

OSHA'S CLAIM THAT PRENATAL EXPOSURE TO ETS AND EXPOSURE TO ETS AS A CHILD MAY INCREASE AN INDIVIDUAL'S CANCER RISK BY A FACTOR OF TWO IS UNSUPPORTED BY A THOROUGH REVIEW OF THE AVAILABLE LITERATURE

In an attempt to substantiate its claim regarding the possible risk of cancer in nonsmokers exposed either prenatally or as a child to ETS, OSHA cites three papers. (Exs. 8-65, 8-164, 8-252) The first study reported an association between exposure to maternal smoking during childhood and an increase in lung cancer risk in nonsmokers in only one subgroup of subjects. Janerich et al., 1990, reported only one statistically significant risk estimate out of 13 exposure categories. The third reference is a reply to a Letter to the Editor regarding the Pershagen 1987 study (which itself is not referenced by OSHA). (Ex. 8-252) The Pershagen study reported "no consistent evidence of an effect," and the 95% confidence interval encompassed 1.0 for both histologic groups. Therefore, the studies' risk estimates were not statistically significant.

The two studies and the Letter to the Editor cited by OSHA examine the potential effect on an individual's cancer risk from exposure to parental smoking during childhood. These studies are therefore irrelevant to a discussion of potential health effects on the fetus from exposure of the mother to ETS in the workplace during her pregnancy. Nonetheless, a reviewer of this literature concluded that "the data do not indicate any association at all between risk of lung cancer in never smokers and exposure to ETS at work, or in childhood."[20]

OSHA PROVIDES A REFERENCE TO ONE EXPERIMENTAL ANIMAL STUDY WHICH IT CLAIMS IS SUPPORTIVE OF THE CONTENTION THAT EXPOSURE OF PREGNANT MOTHERS TO ETS IN THE WORKPLACE PRESENTS A SIGNIFICANT RISK OF MATERIAL HEALTH IMPAIRMENT TO THE FETUS

Although OSHA acknowledges that "experimental research on the adverse reproductive effects associated with ETS exposure in animals is limited," they do report on one study. (Ex. 8-6) This study reported that sciatic nerve tissue taken from the offspring of fresh sidestream smoke-exposed female mice revealed "definite toxic effects" on the neonatal tissue. There are several limitations of this study. Probably the most important is the small sample size. The authors reported data on only six exposed offspring and six controls. In addition, COHb levels of the exposed pregnant mice were 9%, which the authors report is

"equivalent to that found in humans who actively smoke 10-20 cigarettes per day." As one author suggested, studies which simulate mainstream smoke and employ levels equal to or greater than those expected from active smoking generate data which "are not appropriate for assessment of the likelihood or nature of ETS effects." The author also suggested that the authors of such studies should realize that "careful attention must be given to ensure that observed effects are not simply the result of maternal toxicity and systemic stress resulting from excessive doses."[10]

The authors of this study themselves also noted that these reported changes have been observed in other studies, including studies of the diabetic strain of the C57BL/KsJ mouse and in studies of decreased maternal food intake. They concede that "the irregularities noted in our investigation could be attributed to causes other than cigarette smoke inhalation as previous studies demonstrate."

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SECTION X

MATERIAL IMPAIRMENT: GENOTOXICITY

GENOTOXICITY

OSHA FAILS TO JUSTIFY ITS INCLUSION OF GENOTOXICITY AS A SEPARATE CATEGORY UNDER THE MAJOR HEADING OF "HEALTH EFFECTS"; OSHA FAILS TO SHOW THAT GENOTOXICITY IS A MATERIAL IMPAIRMENT TO HEALTH

Genotoxicity refers to damage to DNA (the hereditary material). Permanent, heritable changes in the DNA are called mutations, and may be examined in tests for mutagenicity, such as the Ames test, in which mutation rates are measured in a particular strain of bacteria. Some correlations have been made between mutagenicity and carcinogenicity (the ability to induce cancer).

Other tests used to assess genotoxicity include the sister chromatid exchange (SCE) assay, which measures the frequency of exchange of portions of genetic material between two identical strands of DNA, and the chromosome aberration (CA) assay, which measures structural irregularities in strands of DNA. DNA adducts, abnormal configurations or clumping of the genetic material, may also be examined.

All forms of life are constantly exposed to physical and chemical agents in the environment (e.g., radiation) and to endogenous (internal) agents with the ability to cause changes in DNA. DNA has been called an "unstable" molecule, and it has been

noted that endogenous DNA damage may occur at the rate of 100,000 base pairs per cell, per day.[1,2]

According to Bruce Ames, developer of the Ames assay for mutagenicity, human exposure to potentially mutagenic or carcinogenic substances is much greater than generally appreciated, e.g., the environment can be thought of as "filled with potential carcinogens."[2]

Moreover, conclusions about genotoxicity obtained from in vitro systems, while certainly providing some information about the substance being tested, must nevertheless be put into the proper biological context. The magnitude of a genotoxic response in the whole organism may be substantially different than that observed in a bioassay. As Ames and Gold noted[3]:

> [H]umans have numerous inducible defense systems against mutagenic carcinogens, such as DNA repair, antioxidant defenses, glutathione transferases, and so forth . . . [L]ow doses of carcinogens appear to be both much more common and less hazardous than is generally thought.

Given the ubiquity of mutagens in the environment and the existence of numerous "defense systems" against mutagens, OSHA has not provided sufficient information in the Proposed Rule to support

its treatment of genotoxicity as a "health effect" or to establish genotoxicity as a material impairment to health.

OSHA'S REVIEW OF THE LITERATURE ON THE CLAIMED GENOTOXICITY OF ETS IS INCOMPLETE; A REVIEW OF ADDITIONAL RELEVANT STUDIES PROVIDES NO SUPPORT FOR OSHA'S CLAIM

OSHA's discussion of genotoxicity begins with a series of statements about the claimed correlations between genotoxicity and carcinogenicity. (Section II.C.7., 59 FR 15981) OSHA fails to provide references in support of these statements, although they appear to be OSHA's justification for discussing genotoxicity.

The Proposed Rule then contains a discussion of a number of studies in which cigarette smoke or cigarette smoke condensate was tested in the Ames Salmonella typhimurium assay, and an increased mutation rate was reported. OSHA's inclusion of studies dealing with mainstream and sidestream smoke again reveals the misconception pervading the Proposed Rule that ETS, mainstream, and sidestream smoke are equivalent.

OSHA omitted at least one relevant study from this discussion in the Proposed Rule. In 1991, Bombick, et al., reported on a cellular smoke exposure techniques using rat liver cells and the Ames Salmonella assay. After a three-hour exposure

using ETS at a concentration of 1.5 mg total particulate matter/m^3, the authors report[4]:

> Using the neutral red cytotoxicity and Ames mutagenesis assays there were no differences observed in the ETS-exposed cells and their respective room air controls, indicating that ETS was biologically inactive as tested. [emphasis added]

The Proposed Rule also discusses studies reporting that various constituents and extracts of ETS collected from indoor air are capable of inducing mutations in the Ames assay are also discussed. (Exs. 4-202, 4-5, 4-198, 4-201, 4-203) However, the significance of such reported findings has not been established. Virtually all air samples, whether in the presence or absence of smoking, can be shown to be mutagenic in various bioassays. Indeed, no substance, including foods and natural materials, has been unequivocally shown to be free of mutagenic and/or carcinogenic properties.

Of relevance, a study not cited by OSHA has reported that sidestream smoke exhibits reduced activity as it ages and becomes diluted, that is, as it becomes ETS.[5] Sonnenfeld and Wilson report on an experiment in which cultured mouse fibroblast-like cells were exposed to mainstream or sidestream smoke of various ages. In

this report, cytotoxicity (cell mortality) is used as a measurement of DNA damage sufficient to cause cell death. The authors write:

> Aging of SS smoke resulted in a rapid decline in the mortality generated by the smoke. As calculated from the linear regression curve, an increase in age of SS smoke of 30 [seconds] after generation would have resulted in a total loss of cytotoxic effects. [emphasis added]

The Proposed Rule almost completely overlooks genotoxicity studies using bodily fluids of persons exposed to ETS; these data do not allow a conclusion about genotoxicity to be reached

One area of research essentially overlooked in OSHA's Proposed Rule comprises those studies that have compared the mutagenicity of body fluids of nonsmokers exposed to ETS and nonsmokers not exposed to ETS. Several of these studies report no significant difference in mutagenic activity.[6-10] (Ex. 8-152)

For instance, in research by a team of German researchers, ten nonsmokers were exposed to ETS, generated by human smokers, for eight hours under two exposure conditions.[9] The two experiments were characterized by CO levels of 10 ppm and 25 ppm, respectively; according to the authors, both exposure regimes represent higher exposures than "real-life" situations. Elsewhere,

they described Experiment 2 as "far from being realistic,"[6] and bearing "no relation to a real-life situation."[8] In addition, the authors controlled for the effect of mutagens from the diet by keeping their subjects on a diet low in polycyclic aromatic hydrocarbons. Urine samples from both smokers and nonsmokers were tested in the Ames Salmonella assay. The authors report:[9]

> All urine extracts of ETS exposed non-smokers were found to be negative in the mutagenicity test when applying the [criterion] of Ames (doubling of spontaneous mutation rate).

Thus, even at exposure levels higher than would be expected on average, no increase in mutagenicity could be measured. These data do not support claims that ETS exposure is associated with an increase in mutagenic activity.

Citing the high variability of measures of urinary mutagenicity and questions about the relevance of increased urinary mutagenicity to cancer risk, the authors write:[8]

> These considerations lead to the conclusion that measuring the urinary mutagenic activity, at least in passive smokers, is not an appropriate method of predicting an increased risk to human health.

The authors also say:[8]

> The data suggest that nonsmokers in real-life situations take up very low doses of ETS constituents, and detoxification of the genotoxic substances inhaled is effective.

And:[10]

> Whether ETS exposure can lead to an elevated urinary mutagenicity is a matter of controversy. In most investigations no significant increase has been observed. . . .
>
> In our experience, the Ames test for detection of urinary mutagenicity is far too insensitive to assess such a low exposure. The results of our investigations, as well as those of other authors, suggest that urinary mutagenicity, which would be a potential marker for ETS particle exposure, remains unchanged after ETS exposure.

The few studies reporting statistically significant increases in urinary mutagenicity among individuals exposed to ETS did not employ realistic levels of exposure to ETS, and they did not control adequately for the presence of mutagens in the diet of the study subjects.[11-13] For instance, in the Bos, et al., study, the exposure condition consisted of the smoking of 157 cigarettes over six hours in a room with "poor ventilation."[11] The relevance of such an exposure to "real-life" conditions is certainly questionable. With respect to diet, Bartsch, et al., acknowledge, concerning their study, that[13]

> Urinary mutagenicity is influenced also by dietary habits; although we collected information on diet, the dimension of the study (particularly as far as passive smokers are concerned) does not allow adequate statistical treatment of this potential confounding factor.

Other related studies have examined levels of various DNA changes in nonsmokers exposed to ETS.[1,14-17] (Exs. 8-152, 8-287) Based on the data presented in these studies, nonsmokers exposed to ETS do not appear to exhibit increased DNA adduct formation, nor do studies report increased levels of chromosomal changes in cells of nonsmokers exposed to ETS. Discussion of these studies follows.

Collman, et al., collected data from 16 nonsmokers, 15 "passive smokers" (currently living with one or more smokers), and 13 current smokers, all women.[14] Sister-chromatid exchange (SCE) frequencies in lymphocytes (a type of white blood cell) were compared with and without coincubation with a chemical that enhanced the frequency of SCEs. Based on both assays, the authors report that "the frequency of SCEs in persons passively exposed to smoke was not higher than in nonsmokers."

In a report by Husgafvel-Pursiainen, peripheral blood lymphocytes were examined for SCE frequency.[15] Study groups consisted of 12 smoking waiters and waitresses, 20 nonsmoking waiters and waitresses who were occupationally exposed to ETS, and

14 nonexposed office workers. The author reports that "[t]he mean SCE level in exposed non-smokers did not differ from that observed in the non-exposed group." Although no ETS measurements from the restaurants were reported, the author characterizes them as "heavily polluted," and the exposure as "long-term." This study, which reports data from persons exposed in a "real-life" situation, does not support claims of the genotoxicity of ETS.

Chromosomal aberrations (CAs) and SCEs were examined in peripheral blood lymphocytes from nine smoking waiters, 16 nonsmoking waiters exposed to ETS at work, and 7 reportedly nonexposed nonsmokers by Sorsa, et al. (Ex. 8-287) The authors report that "[n]o significant differences were seen between the groups or subgroups in the 2 parameters." Thus, no "genotoxic" effects could be detected in persons exposed to ETS at "real-world" levels.

Holz, et al., report that DNA adduct levels were compared in monocytes (a type of white blood cell) of smokers and "heavily exposed passive smokers," who had been exposed in a chamber.[16] DNA adducts above background were reported in smokers; they disappeared in less than 40 hours. The authors report no above-background adduct levels in study subjects exposed to ETS.

In a study by Gorgels, et al., 50 self-reported ETS-exposed men ("passive smokers"; average 72.8 hours exposure per week) were compared with 56 self-reported low ETS-exposed men (average 5.1 hours per week).[17] SCEs in cultured lymphocytes were examined; the authors reported that "[n]o difference was observed between low exposed non-smokers and the passive smokers." They concluded:

> Our results are in accordance with previous smaller studies in less homogeneous populations of non-smokers. These studies also failed to demonstrate even a tendency for an association between passive smoking and SCE levels. . . .

Five male smokers, five male nonsmokers, and five male nonexposed nonsmokers were compared in Holz and colleagues' 1993 paper.[1] The endpoint examined was DNA single-strand breaks (SSBs), "considered to be an important parameter of genotoxic stress," in lymphocytes. The authors write:

> All probands revealed measurable and varying SSB levels. Since DNA is an unstable molecule and estimated endogenous damage exceeds 100000 affected base pairs per cell per day, we assume that SSB base levels reflect unrepaired lesions. Active smoking caused an increase in SSBs in peripheral blood lymphocytes. This effect could not be found in passive smokers . . .

ETS exposure in this study consisted of five smokers each smoking 24 cigarettes in eight hours in an exposure chamber. This study provides no support for claimed genotoxic effects of ETS, even at a high exposure level.

Conclusion

This review of data from studies in which genotoxicity was assessed in persons actually exposed to ETS thus provides little, if any, support for the contention that ETS is genotoxic at levels encountered in workplaces and other indoor environments.

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SECTION XI

THE PROPOSED RULE ON ETS:

FEASIBILITY AND ALTERNATIVES

OSHA'S PROPOSED RULE ON ETS: FEASIBILITY AND ALTERNATIVES

OSHA HAS NOT DEMONSTRATED ANY CONTRIBUTION OF ETS TO CONSTITUENT LEVELS ABOVE BACKGROUND LEVELS IN THE WORKPLACE; OSHA HAS NOT MADE A DETERMINATION OF "SIGNIFICANT RISK" FOR AMBIENT ETS EXPOSURE LEVELS; OSHA FAILS TO PROVE THAT ETS CANNOT BE ADDRESSED THROUGH PROPER VENTILATION; OSHA FAILS TO EXPLORE ALTERNATIVES TO SMOKING BANS

OSHA states that the "primary objective of the tobacco smoke provision is to eliminate the nonsmoker's exposure to ETS. Under the Proposed Rule, firms will have the option of either banning smoking of tobacco products or permitting smoking only in designated areas." (59 FR 16016) The designated smoking area must be completely enclosed with a separate exhaust directly to the outside. In addition, the area must be negatively pressurized to prohibit exposure of any ETS constituent outside the designated area. (59 FR 16029) The Proposed Rule on ETS, according to OSHA, reduces "significant risk of material health impairment to the extent feasible." (59 FR 16013)

The Proposed Rule, however, does not explain why the complete elimination of ETS is required or how the studies that OSHA selected for its analysis of significant risk warrant the complete elimination of ETS. According to a recent court opinion (AFL-CIO v. OSHA, 965 F.2d 962, *975), OSHA's determination that a

new standard is "reasonably necessary or appropriate" and that it "most adequately assures . . . that no employee will suffer material impairment of health or functional capacity, . . . necessarily requires some assessment of the level at which significant risk of harm is eliminated or substantially reduced." OSHA does not provide an assessment of the level of "significant risk of harm." That is because its analysis of significant risk for ETS is based upon two epidemiologic studies that are inconsistent with the body of evidence on health effects from workplace exposures to ETS, and from which estimated risks are generated without reference to actual ambient measures of ETS exposures.

OSHA provides no reason for setting its ETS standard at "zero" exposure. The zero level of exposure does not follow from OSHA's analysis of significant risk. It does not follow from OSHA's contention that its ventilation-based IAQ standard will not be effective in the removal and dilution of ETS constituents because "air exchange rates in non-industrial workplaces are not designed to control the risks of ETS exposure" (59 FR 15991), or because "the carcinogenicity of ETS discounts the use of general ventilation as an engineering control for this contaminant." (59 FR 15992) As discussed in Section IV of this submission, ordinary air in public places and workplaces contains many of the same substances imputed to ETS, in the complete absence of smoking.

Such substances, some of which are designated as "carcinogens" by OSHA, are produced by many common sources, and complete removal of ETS from the ambient air will not eliminate exposures to them. Moreover, some individual constituents found in both indoor air and ETS are already regulated by OSHA. OSHA establishes permissible exposure levels to such airborne substances presumably at levels protective of employee health and at which no significant risk of material impairment exists. The levels of exposure are typically far greater than any actually generated by ETS. OSHA's own Proposed Rule on IAQ does not call for the complete elimination of such substances, some of which are "carcinogens," but for the reduction of exposures to an "acceptable" level by ventilation.

OSHA thus has not demonstrated the extent to which ETS contributes to constituent levels above background levels in the workplace, it has not made a determination of "significant risk" for ambient ETS exposure levels, and it fails to prove that ETS cannot be addressed through proper ventilation, as spelled out in its own IAQ standard.

While the complete elimination of ETS is achievable through a smoking ban,* the complete elimination of the same

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*. OSHA's rulemaking on ETS is directed at stopping the smoker rather than "protecting" the nonsmoker. A smoking ban with the express purpose of altering smoking behavior may be seen

(continued...)

constituents from other sources is not possible. If a comprehensive indoor air quality standard were truly the goal of the Proposed Rule on IAQ and ETS, then OSHA would have explored alternatives that are functionally equivalent in effectiveness to smoking bans in the reduction of exposures to ETS -- alternatives that would not seek to alter the behavior of the smoking workforce. A discussion of alternatives to smoking bans and/or separately ventilated smoking rooms follows below.

Current design and operation criteria for ventilation provide for the effective dilution and removal of ETS constituents from workplaces in which smoking is unrestricted; a ventilation Standard, ASHRAE 62-1989, has been incorporated into the major building codes in the U.S.; since 1990, the Standard has provided design and operations criteria for ventilation systems in new, remodeled and renovated buildings; the Standard has been incorporated by reference into OSHA's Proposed Rule on IAQ

The Proposed Rule states, without justification, that ventilation cannot be used to address the "risks" purportedly associated with exposures to ETS. The Proposed Rule specifically cites the "failure" of ASHRAE Standard 62-1989 in the "elimination" of "risks" from ETS exposures. (59 FR 15992) While ASHRAE Standard 62-1989 does not explicitly address purported "risks" from indoor air exposures, it establishes ventilation rates for various

*.(...continued)
as an attempt at "social engineering" and clearly is not, and ought not to be, within OSHA's regulatory framework.

locations in order to "control carbon dioxide and other contaminants with an adequate margin of safety, and to account for variations among people, varied activity levels, and a moderate amount of smoking" [emphasis added].[1] The Chairman of the ASHRAE Standards Project Committee for Standard 62-1989, Mr. John Janssen, writes:

> Laboratory research at Yale University and at the Technical University of Denmark has shown that 15 cfm of outdoor air will dilute occupant odors to a level acceptable to at least 80 percent of the people entering an occupied space from outdoors. Research on tobacco smoke odor at Yale's John B. Pierce Laboratory has also shown that with today's reduced smoking rate 15 cfm of outdoor air will dilute environmental tobacco smoke to a level acceptable to 70 percent of the people entering an occupied space where about 27 percent of the occupants smoke at a rate of 1.25 cigarettes per hour. This equates to one pack per 16 hour day. Other calculations on the tobacco smoke perception of nonsmoking occupants in a room for 15 minutes with smokers show that nonsmoking occupants will register 90 percent acceptance under the assumed conditions. Thus, Standard 62-1989 appears to be able to control tobacco smoke odor under minimum smoking conditions.[2]

The minimum ventilation rate recommended by ASHRAE Standard 62-1989, 15 cfm outside air/person, is the level at which odors, metabolic byproducts, and ETS are effectively diluted and removed.[3-5] (Ex. 3-440) The effectiveness of the minimum ventilation rate for the dilution of ETS has been evaluated by scientists.[6-8] In 1990, Pedelty and Holcomb demonstrated that air

quality in areas where smoking is permitted ad lib does not differ significantly from the quality of air in nonsmoking areas, where both areas are supplied with the minimum outdoor air ventilation rates recommended in ASHRAE 62-1989.[6]

In their review of ETS-related air quality monitoring in different workplaces under various smoking conditions, researchers from TDSA Ltd. conclude "in office areas in which (a) smoking is allowed and (b) outside air ventilation rates meet or exceed the ASHRAE Ventilation Standard, nicotine concentrations have typically been less than 5 ug/m^3 and respirable suspended particles have ranged between 20 ug/m^3 and 60 ug/m^3.[7] (Ex. 3-1073)

In their submission to the OSHA RFI Docket, scientists summarized the results of their paper on the measurement of ETS in 585 offices. (Ex. 3-1053) The authors write:

> Computer analysis shows that when "blind-folded" for presence or absence of smokers, in most cases realistic smoking levels do not significantly influence the aspects of air quality that were measured, and spillover from smoking areas into nonsmoking areas appears to be minimal. This work further reinforces the position the American Society of Heating, Refrigerating and Air-Conditioning Engineers has taken on ETS in office buildings in ASHRAE Standard 62-1989, that acceptable air quality can be maintained in properly ventilated offices with a moderate amount of smoking even without smoker segregation.

Professor Alan Hedge offers the following observation on the basis of his extensive experience in monitoring ETS constituents during investigations of sick-building syndrome: "Our data show that modern ventilation systems are capable of diluting the small pollutant loads from smoking at the levels which we observe, without necessarily exposing nonsmokers to significantly elevated levels of indoor air pollutants." (Ex. 3-955)

Company scientists from R.J. Reynolds (RJR) reported on a recently completed study of four office buildings.[8] (Ex. 3-1087) Two of the buildings investigated had a policy of unrestricted smoking and, in two other buildings, smoking was restricted to separately-exhausted lounges. Regardless of smoking policy, RJR reports that ventilation and indoor air quality indicators were "well within applicable standards." The authors write:

> In summary this study demonstrates conclusively (a) that with a HVAC system that is adequately designed, operated in accordance with current ASHRAE standards and properly maintained, all indicators for ETS are at extremely low, de minimis levels, even in the presence of substantial smoking activity, and (b) that such smoking activity has a negligible effect on contaminant levels in buildings where smoking is unrestricted.

They conclude:

> RJR believes, based on its own detailed research and the consistent results of other workplace assessments, that a properly designed and maintained HVAC system that is

operated in accordance with the ventilation rate procedures of the ASHRAE Standard 62-1989, will be effective in assuring that exposures to ETS will be de minimis.

Thus, in buildings meeting the ventilation rates specified in ASHRAE 62-1989, return air from areas in which smoking is permitted will be diluted by outside air, and the mixture of return and outside air will be filtered prior to returning to the supply system. The dilution factor accounts for the low levels of ETS constituents measured in nonsmoking areas, as documented in the above studies.

Simple physical separation of smokers and nonsmokers has been effective in the reduction of nonsmoker exposure to ETS; simple spatial separation of smokers and nonsmokers, even under conditions of recirculated ventilation, effectively minimizes ETS exposure for nonsmokers; data do not support a significant reduction in ETS exposures beyond adequate ventilation and/or simple separation of smokers and nonsmokers

Scientific studies indicate that the simple physical separation of smokers and nonsmokers, even under a shared ventilation system with recirculated air, can effectively minimize nonsmoker exposures to ETS.[7,9-20] Other studies indicate that smoking bans and/or separately ventilated smoking areas do not significantly reduce ETS exposures beyond reductions achieved through simple separation and/or adequate ventilation.[8,9,12-14,17]

A 1990 study by Vaughn and Hammond, cited in the Proposed Rule (59 FR 15991), examined the impact of smoking policies on ETS constituent levels in a high-rise building.[9] The authors reported an 80 percent reduction in exposure to ETS constituents in nonsmoking workareas after designation of a smoking area on a floor that utilized a common (recirculating) air-handling system. Exposure levels to nicotine in nonsmoking workareas prior to the designation of the smoking area were 2.0 ug/m^3; after institution of the smoking policy, nicotine levels dropped to 0.1-0.3 ug/m^3. A complete smoking ban on another floor in the building produced a 95+ percent reduction in ETS constituents, only a 15 percent exposure reduction beyond simple separation of smokers and nonsmokers.[9]

Another study of a smoking-restricted office building reported that ambient nicotine in nonsmoking areas was virtually undetectable.[10] Smoking was restricted to designated areas with local air filtration systems. The authors concluded that spatial restrictions are "effective in minimizing the impact of environmental tobacco smoke on indoor air quality."[10]

In a similar study, Canadian researchers compared measured ETS constituents in offices where smoking was regulated and unregulated.[7,11] They reported no significant differences in average ETS constituent levels between nonsmoking offices that

received recirculated air from designated smoking areas, and nonsmoking offices that did not receive recirculated air. Nicotine concentrations reported for nonsmoking areas were only marginally above limits of detection and quantitation; there were no measurable differences in particles or carbon monoxide levels in nonsmoking areas that did or did not receive recirculated air from smoking areas. The researchers concluded:

> The results indicate that the provision of a designated, but not separately ventilated, smoking area can effectively eliminate or drastically reduce most components of environmental tobacco smoke for nonsmoking offices.[11]

In 1991, Hedge, et al. examined the effects of smoking policies on indoor air quality in 18 private-sector buildings.[12] The study covered over 3,000 workers. They concluded:

> Comparison of all open-office sites between policies showed no significant differences in levels of carbon monoxide, carbon dioxide, formaldehyde or respirable particulates. . . . Smoking policy had a relatively small effect on IAQ for the pollutants measured. For most of these pollutants, there were no significant differences in concentrations among offices in SP (smoking-prohibited) buildings, nonsmoking office areas in RF (smoking restricted to rooms with local filtration), RSV (smoking restricted to rooms with separate ventilation) and RMP (smoking restricted to rooms with no location air treatment) buildings, and office areas in RWS (smoking restricted to open-plan cubicle workstations and enclosed office) buildings. There was a significant effect of smoking policy on UVPM and formaldehyde in these office areas . . . however, all

concentrations of UVPM and formaldehyde were low.

A 1993 follow-up study by the same authors compared ETS constituent levels in 27 office buildings under five different kinds of smoking policies.[13] The smoking policies ranged from unrestricted smoking to the complete prohibition of smoking. The authors report that nicotine and tobacco-specific particles (UVPM-RSP) were measurable in offices that permitted smoking, but exposures to other airborne substances were similar across all buildings, regardless of smoking policy. The authors estimated that a typical nonsmoker would be exposed to the nicotine equivalent of approximately three cigarettes per year in open-plan offices with smoking restricted to enclosed parameter offices. Simple separation of smokers and nonsmokers under a common ventilation system was estimated to result in nicotine exposure levels of no more than five cigarette equivalents per year.

A 1993 Canadian study compared exposures to ETS constituents in three buildings before and after smoking bans.[14] The authors reported a significant reduction in average levels of volatile organic compounds in the buildings after the smoking ban, a result they could not explain and one that is inconsistent with other studies that demonstrate no significant contributions from ETS to indoor levels of total volatile organic compounds.[15,16] The smoking ban, however, had no significant effect on overall

exposures to carbon monoxide or particles, or on cotinine levels in body fluids of nonsmokers.

Similarly, Proctor (1987) monitored ETS constituents before and after a smoking ban on public transportation in the United Kingdom.[17] While nicotine concentrations decreased from 7 ug/m^3 to 3 ug/m^3 in nonsmoking compartments after the ban, particulate and carbon monoxide levels remained unchanged. This suggests that ETS contributions to levels of particulate and CO in public transportation are not significant.

In another study by Proctor and co-workers (1989), the researchers measured nicotine, RSP, carbon monoxide, carbon dioxide, and volatile organic compounds in the air of smokers' and nonsmokers' offices.[15] The data indicate little nonsmoker exposure to various ETS constituents through simple separation. The average UVPM-RSP level in nonsmokers' offices was 8.8 ug/m^3; the median nicotine value was less than 1 ug/m^3. Carbon monoxide and carbon dioxide levels did not differ appreciably between smokers' and nonsmokers' offices. Overall, levels of volatile organic compounds did not differ significantly between smokers' and nonsmokers' offices.

Bayer and Black (1987) reached a similar conclusion in their investigation of volatile organic compound levels in smokers'

and nonsmokers' offices.[16] They noted that although differences in nicotine concentrations were measurable for offices of smokers compared with nonsmokers, no significant differences in volatile organic compounds were discerned in smokers' and nonsmokers' offices. The researchers observed that "it was not possible" to correlate volatile organic compounds with ETS or to attribute the source of various volatile organics to ETS.

A 1989 study performed for the U.S. Department of Transportation on ETS constituent levels aboard commercial aircraft indicates the overall effectiveness of simple separation of smokers and nonsmokers in the minimization of ETS exposures.[18] This study is cited in the Proposed Rule. (59 FR 15991) The researchers reported an average level of 0.11 ug/m^3 nicotine in nonsmoking sections for their sample of 61 domestic commercial flights. The average level was over 100 times lower than that measured in smoking sections; it is equivalent to 1/8000 the nicotine delivery of a single cigarette.

In the largest study of its kind, researchers reported measurements of ETS constituents in 585 offices, many of which were conventional office settings with simple separation of smokers and nonsmokers under common air-handling systems and recirculated air.[19] The researchers concluded that: "[I]n most cases realistic smoking levels do not significantly influence the aspects of air quality

that were measured, and spill-over from smoking areas to nonsmoking areas appears to be minimal." "Spill-over" of tobacco smoke constituents was reported in only four percent of the nonsmoking areas.

Lambert, et al. (1993) examined differences in nicotine and RSP levels in the nonsmoking and smoking sections of restaurants.[20] Simple separation of smokers and nonsmokers in restaurants resulted in substantial reductions of exposure to RSP and nicotine for nonsmokers. Nicotine concentrations averaged 65 percent lower in nonsmoking sections than in smoking sections; RSP concentrations were 40 percent lower. The average concentration of nicotine in smoking areas was 3.2 ug/m^3 compared with 1.0 ug/m^3 in nonsmoking areas. The difference between average RSP levels in smoking and nonsmoking sections was 26 ug/m^3, a level consistent with those reported for the contribution of ETS in homes and in offices with smokers. (See Table V, Section IV)

The studies reviewed above contain data regarding the low levels of ETS constituents in nonsmoking areas under conditions of simple separation of smokers and nonsmokers with recirculation of ventilation air. Data reported in those studies indicate that ETS constituent levels in nonsmoking areas in buildings where smoking is permitted are often only slightly above limits of detection and quantitation, and often statistically indistinguishable from

"background" levels of such constituents found in buildings in which smoking is altogether prohibited. The data support the contention that simple physical separation of smokers and nonsmokers effectively reduces and minimizes ETS exposure in nonsmoking areas, even under conditions of recirculated ventilation.

There are substantial data, submitted to the OSHA RFI docket on IAQ and reviewed in this section, that indicate that typical workplace exposures to ETS constituents are low and reducible to de minimis levels through the simple physical separation of smokers and nonsmokers in conjunction with the current ventilation rates adopted in OSHA's Proposed Rule on IAQ. **The Proposed Rule provides no discussion or scientific data that would support a finding that ETS is related to any material health impairment at exposure levels encountered through simple separation and/or adequate ventilation.**

Negative air pressure zones; if physical grouping of smokers and nonsmokers in discrete areas is desired by employers, prevailing air circulation currents and routes of supply and exhaust air should be considered; if possible, smoking areas should be placed near existing exhausts so that air movement will be directed from nonsmoking to smoking areas, thereby minimizing possible migration of tobacco smoke from smoking areas

According to Hayward, et al. (1993), the effectiveness of a designated smoking area for controlling exposure to ETS in nonsmoking areas is determined by two basic factors.[21] The first requires the successful dilution and removal of ETS constituents within the smoking area. The ventilation rate, either through outside air or transfer air (the air from other zones within the building), is the most critical determinant for the dilution and removal of ETS constituents. Outside air should be supplied at rates designated by ASHRAE Standard 62-1989.

A second factor related to the movement of ETS constituents from smoking areas to nonsmoking areas depends upon airflows within the structure.[21] Airflow is affected by the existence of physical barriers such as walls or partitions, as well as by air pressure relationships within the building. For a designated smoking area without partitions, the simple location of smokers near existing exhausts and the designation of nonsmoking areas near supply air diffusers will prevent movement of ETS constituents into nonsmoking areas. Airflow will be directed from

the nonsmoking or supply air areas into smoking areas, thereby preventing the air from the smoking area from re-entering that of the nonsmoking area. This technique, known as "air pressure zoning," has been described in a recent publication for design engineers:

> Air generally flows from areas of higher air pressure to areas of lower air pressure, from positive pressure in the direction of negative pressure. Using this simple concept, areas set aside for nonsmokers can be maintained at a slight relative positive pressure, while areas set aside for smokers can be maintained at a slight negative relative air pressure. This will produce a slight airflow from the nonsmoking area into the smoking area, keeping the air from the smoking area from mixing with that of the nonsmoking area. Through thoughtful planning and carefully supervised and tested balancing of the HVAC system, the preferences of both smokers and nonsmokers can be accommodated without any additional cost to building operations.[22]

Air pressure zoning involves the use of existing ventilation systems, e.g., supply and exhausts within a building, and will not influence capital costs or operating efficiencies for a building.

An alternative to the separate smoking area required in the Proposed Rule (i.e., an enclosed space with dedicated exhaust under negative pressure) utilizes the theory of negative pressure and the use of transfer air, which is air drawn directly from other parts of an occupied space. The use of transfer air in a practical

smoking lounge design is permitted under ASHRAE Standard 62-1989. The lounge would be ventilated in a way similar to the way restrooms are ventilated and exhausted. Restrooms in public buildings are equipped with exhaust ventilation for the removal of odors, etc. The restroom often draws its supply air from adjacent areas such as corridors that are close to the restroom. The rooms adjacent to the restroom are not fitted with comparable exhaust capabilities. The exhaust air from the restroom creates a negative pressure relative to its adjoining areas. Air is thus "transferred" from adjacent areas of positive pressure into the restrooms and, if the exhaust is working properly, the result is the creation of a negative pressure zone.

The 1993 publication by Hayward, et al. examined the effect of negative pressurization on movement of ETS constituents in three separate buildings.[21] In one of the buildings, the use of a small exhaust fan in the smoking area dramatically reduced migration of ETS constituents into nonsmoking areas. Exposures to nicotine and RSP in nonsmoking areas were reduced below the limit of quantitation. In a second building, the effects of negative pressurization were less dramatic because the ventilation was very effective from the outset in removing and diluting ETS constituents. A third building was not negatively pressurized in smoking areas and nonsmoker exposure to ETS constituents was greater than in the other two buildings.

In 1993, Light and Gay measured nicotine levels in two office buildings with a variety of areas designated for smoking.[23] Nicotine was below the level of detection (less than 0.7 ug/m^3) in most of the sites measured. The authors concluded: "Within the sensitivity of the tests and observations performed, exposure was not documented from the recirculation of air even though many smoking areas were not exhausted to the outside. This suggests that there was little, if any, hazard under the conditions evaluated in areas potentially receiving recirculated ETS but not immediately adjacent to smoking." They reported that "positive pressurization of smoking rooms" led to "intermittent nonsmoker exposure in immediately adjoining areas." If the smoking areas were negatively pressurized, no detectable exposure to ETS constituents occurred adjacent to smoking areas.

Feasibility of OSHA's Proposed Rule on ETS

According to OSHA, "the primary objective of the tobacco smoke provision [of the Proposed Rule] is to eliminate the nonsmoker's exposure to ETS." (59 FR 16016) OSHA further states: "Under the Proposed Rule, firms will have the option of either banning smoking of tobacco products or permitting smoking only in designated areas." (59 FR. 16016) The Proposed Rule requires that designated smoking areas be enclosed, exhausted directly to the outside and maintained under negative pressure. (59 FR 16032)

Under OSHA's Proposed Rule for ETS, constituents imputed to ETS will be "eliminated" from the workplace, while exposures to the same constituents from other sources will be minimized to presumably acceptable levels by the ventilation-based Proposed Rule for IAQ. The foregoing analysis clearly demonstrates that: (1) ETS constituent levels in typical workplaces are low and nonsmoker exposure to ETS constituents is minimal; (2) simple physical separation of smokers and nonsmokers in the workplace provides for significant reductions of already minimal exposures to ETS constituents; (3) adequate ventilation effectively dilutes and removes ETS constituent levels to the extent that levels will often fall below levels of detection or quantitation and will not differ significantly from background levels of constituents generated by other sources; and (4) the negative pressurization of smoking areas will prevent "migration" or "spillover" of ETS constituents into nonsmoking areas.

OSHA's proposal to completely eliminate ETS constituents is a regulation that seeks to modify already insignificant levels of ETS exposure. The alternatives described above were not considered by OSHA, yet they are equivalent in effectiveness to OSHA's proposed requirement of a separately enclosed, separately exhausted, and negatively pressurized smoking room. **The Proposed Rule will produce only trivial and insignificant reductions in**

exposures to ETS constituents over the alternative provisions specified above.

OSHA's Proposed Rule on ETS ostensibly provides a choice regarding smoking for the nation's employers: either ban smoking or construct special smoking rooms. However, the choice is not real. The Proposed Rule constitutes a de facto ban on smoking because OSHA trivializes and minimizes the economic and technological feasibility of providing separate rooms for smoking employees. The "option" of providing a separately ventilated smoking room lies with employers (not building owners), even when the employer leases space for his or her business. OSHA clearly recognizes this impossible scenario in its Proposed Rule, e.g., "since changes in building ventilation systems will be made by landlords, employers may have to negotiate agreements to ensure that they can meet the OSHA Standard. On the requirement for ETS, landlords in turn are likely to pressure employers to ban smoking; thereby forestalling any need for construction of designated smoking rooms." (59 FR 16013)

OSHA declares that problems concerning the technological feasibility of the Proposed Rule "are not evident." (59 FR 16013, 16023) However, the isolation of smokers in a separate room as required by OSHA's Proposed Rule places additional demands on an existing ventilation system. The Proposed Rule's requirement of a

separate exhaust leading directly to the outdoors is not feasible in many buildings.[22] Few existing buildings, particularly high-rise buildings, are amenable to providing exhaust directly to the outdoors from any given location within the building. The option is not technologically feasible in these instances, and the employer, under OSHA's Proposed Rule, would have no choice but to completely ban smoking. The Proposed Rule concedes: "OSHA recognizes that not all establishments will make available designated smoking areas as there may be physical constraints on the option of providing separate ventilation. Such constraints are imposed by the building's design, the building's mechanical ventilation system's capabilities, by cost involved in providing adequate ventilation, by the occupant use of the building." (59 FR 16016) The U.S. EPA recently conceded that "the structural features of many existing buildings make it infeasible or cost prohibitive to construct a smoking lounge" similar to that envisioned by OSHA.[24] The EPA report suggests that smoking lounges would be feasible in only 10 to 20% of the existing buildings in the U.S. Tenants in 80 percent or more of existing buildings would be forced to ban smoking altogether under OSHA's Proposed Rule.

OSHA has placed the burden of its Proposed Rule on ETS upon the nation's employers by presenting them with a "choice" over which they are not empowered (i.e., to ban smoking or restrict it to a specially ventilated room). For the employer who is not also

a building owner, there is no real choice in the matter. For either the tenant or owner of a multi-story building, there may be no "choice" in the matter due to feasibility restrictions. For the small business owner who must lease additional space for a smoking lounge, there may be no "choice" in the matter. For other businesses, retrofit requirements for the construction of an enclosed, separately exhausted and negatively pressurized smoking room may be cost-prohibitive, and the "choice" in the matter disappears. The Proposed Rule does not address these issues.

The minimum outdoor air ventilation rates required in OSHA's Proposed Rule on IAQ are based on versions of ASHRAE Standard 62 (for ventilation); the current ventilation standard, ASHRAE 62-1989, provides minimum outdoor air ventilation rates for ETS; the precursor standard, 62-1973, specified recommended ventilation rates comparable to ASHRAE 62-1989 and served as the ventilation basis for building codes since 1973; OSHA's ventilation recommendation for IAQ will therefore adequately address ETS; OSHA's separation of ETS from general IAQ has no basis

OSHA's Proposed Rule for IAQ (to the exclusion of ETS) states that "employers [must] maintain and operate the HVAC system to provide at least the minimum outdoor air ventilation rate, based on actual occupancy, required by the applicable building code, mechanical code, or ventilation code in effect at the time the facility was constructed, renovated, or remodeled, whichever was most recent." (59 FR 16026-27) In the foregoing analysis, it was

demonstrated that, contrary to OSHA's contention regarding the inapplicability of ventilation to ETS, ASHRAE Standard 62-1989 for Ventilation was specifically designed for, and has been proven successful in, the dilution and removal of ETS constituents. The Standard currently provides ventilation design/operation criteria for building codes in the U.S.

A precursor standard to ASHRAE 62-1989, ASHRAE Standard 62-1973, recommended a ventilation rate of 15 cfm outside air/person, comparable to the minimum recommended outdoor air rate specified in ASHRAE 62-1989. Standard 62-1973 was approved by the American National Standards Institute (ANSI) and incorporated into building codes. It was in effect through the 1970s. ASHRAE updated Standard 62-1973 in 1981 and provided for two ventilation rates based on smoking and nonsmoking (Standard 62-1981). That Standard did not receive approval from ANSI and was not incorporated into the major building codes in the U.S. ASHRAE 62-1973 thus remained in effect throughout the 1980s as the design and operational criteria document for ventilation in building codes. Many HVAC systems designed and installed over the past 20 years have complied with the specifications in ASHRAE 62-1973 and ASHRAE 62-1989.

The ASHRAE Standards (62-1973 and 62-1989) designate the required outdoor air portion of total supply air, where total

supply air equals outside air and return air. The minimum outdoor rates specified in the Standards actually constitute only a fraction of the supply air needed to provide proper heating and cooling; outside air supply requirements constitute a small percentage of the air needed for total supply air. If outside air specifications differ from Standard to Standard, overall HVAC capacities, as determined by minimum design criteria for supply air, would satisfy the demand for greater outdoor air flow rates. Indeed, recent research on 160 office buildings by Sundell, et al. indicated that buildings of different age categories did not differ operationally with regard to outdoor air flow rates.[25] The assumption that an increase in outside air ventilation rates would require the redesign and retrofit of an existing ventilation system is not supported.

Differences in minimum outside air requirements between the two versions of the ASHRAE Standard are not likely to be significant and may, in fact, be identical for certain indoor areas. **Thus, compliance with the Proposed Rule's requirements for minimum outdoor air ventilation rates for IAQ, insofar as they are based on the 1973 and 1989 versions of the ASHRAE Ventilation Standard, would be sufficient to satisfy the ventilation requirements for the effective dilution and removal of ETS constituents under ad lib smoking situations.** There are no feasibility constraints based on compliance with current building

code specifications for ventilation, as specified in OSHA's general ventilation recommendation for IAQ.

As OSHA's Proposed Rule on ETS tacitly admits, an enclosed, separately exhausted and negatively pressurized smoking room is neither technologically nor economically feasible as a real option available to all of the nation's employers. (59 FR 16016, 16013) As demonstrated above, negative pressurization is feasible using existing exhaust and supply locations in a building. A requirement for a separate exhaust from a smoking area directly to the outside is burdensome, superfluous and dictated only by OSHA's "zero exposure" doctrine for ETS. Scientific studies and IAQ reports indicate that smoking and nonsmoking areas may share a common air handling system with recirculation of air such that constituents from ETS from smoking areas are not significantly redistributed to nonsmoking areas. This condition can be achieved if the building conforms to the specifications for ventilation rates and filtration recommended by the current ASHRAE Standard for ventilation -- indeed, by OSHA's own Proposed Rule on IAQ.

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